Junior Management Science 9(4) (2024) 2024-2049

Junior Management Science

www.jums.academy
ISSN: 2942-1861

Road to a Bioeconomy in the European Union: Mapping Drivers of Precision Fermentation Adoption

Niklas Thomas Starz

WHU - Otto Beisheim School of Management

Abstract

The escalating crisis of climate change, biodiversity loss, and pollution necessitates urgent shifts in production and consumption patterns towards enhanced environmental efficiency (EE). Western governments, including the European Union (EU), advocate transitioning to a bioeconomy based on renewable resources and free from fossil fuels. A pivotal technology in this shift is precision fermentation (PF), which employs synthetic biology to transform microbes into 'cell factories' capable of producing diverse goods from renewable feedstocks. Despite its introduction in 1982, PF's impact on EU production processes has been limited. This paper, drawing on Geel's (2002) concept of technology transformations as sociotechnical phenomena, explores the drivers and barriers to PF adoption through interviews with eight biomanufacturing ecosystem experts. Findings reveal a dynamic niche propelled by advances in synthetic biology, environmental pressures, and global supply chain disruptions. However, substantial internal barriers at both niche and system levels hinder transformative progress, underlining critical areas for EU policy intervention. This paper provides strategic insights for policymakers, established companies, and entrepreneurs aiming to navigate the transition to a bioeconomy.

Keywords: biomanufacturing; EU bioeconomy strategy; multi-level perspective; precision fermentation

1. Introduction

In 2023, humanity faces the triple planetary crises threatening the security and survival of numerous living beings on earth: climate change, loss of biodiversity, and pollution of water, soil, and air (IPCC, 2023; UNCCD, 2022; UNEP, 2022). These crises, primarily driven by human production and consumption patterns (Unruh, 2000), demand urgent action and a reevaluation of our economic systems (Elzen et al., 2004). With growing global populations and increasing demands for food, materials, and energy (World Bank, 2023), the pivotal question arises: How can humanity maintain or even enhance its quality of life without exacerbating its detrimental impact on planetary health?

At its core, this concern demands a dramatic improvement in environmental efficiency[1] (EE), – and although incremental innovation and optimization can contribute to improvements, Weterings et al. (1997, as cited in Geels, 2006) suggest that system innovation may be necessary for a substantial leap forward (see Figure 1).

The bioeconomy, an economic model primarily based on renewable and biological resources, offers a potential pathway towards system innovation. Enabled by synthetic biology and industrial biotechnology, the bioeconomy aims to transform value chains for goods that contribute significantly to environmental destruction, such as consuming fossil fuels and raising animals for meat and dairy production. Precision Fermentation (PF), a technology that employs synthetic biology tools to transform microbes into "cell factories" for producing a wide array of known and novel molecules at industrial scales, holds great promise in transforming these sectors while addressing environmental challenges. As an example, the required whey protein for a liter of cow's milk produced via PF could require up to 99% less freshwater (EE factor 100) and emit up to 97% fewer greenhouse gas emissions

[1] Environmental efficiency refers to a system's ability to minimize its environmental impact while maximizing its output or productivity (Korhonen et al., 2018).

DOI: https://doi.org/10.5282/jums/v9i4pp2024-2049

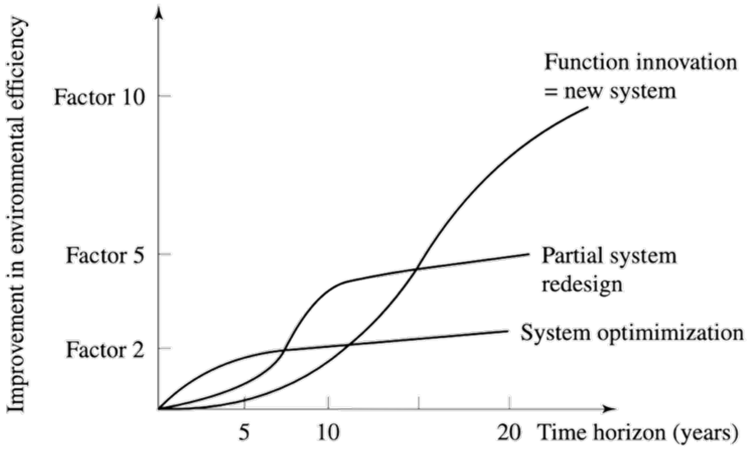

Figure 1: Environmental Efficiency and System Innovation
(Source: Weterings et al. (1997) as cited in Geels (2006))

(GHG) (EE factor 33) than from the actual cow (Perfect Day & WSP USA, 2021; Poore & Nemecek, 2018). Consequently, environmental activist and columnist George Monbiot has touted it as potentially "the most important green technology ever" (Monbiot, 2022).

As one of the world's most influential economies, the European Union (EU) is actively pursuing a more sustainable future, including the transition to a bioeconomy. This ambition is prominently demonstrated by its initiatives, such as *The European Green Deal* (European Commission, 2019) and *The EU's bioeconomy strategy* (European Commission, 2018). However, the initiatives might not be sufficient in the given timeframe (IPCC, 2023), raising the research question: How can the transition to a bioeconomy that involves PF be accelerated? Therefore, this thesis examines the principal current drivers and barriers influencing the development of system innovation in the form of a technology transition.

Past technology transitions demonstrate that it is insufficient to limit the analysis of system transformation to technological drivers. These transitions are driven by a wide range of societal flows and stages, requiring an interdisciplinary approach and a socio-technical lens (Geels, 2006). By employing Frank Geels' (2002) *Multi-Level-Perspective* framework, this thesis explores the potential technological transformation of animal-based protein, materials, and fuel production through the widespread adoption of PF. To gain a comprehensive understanding of these dynamics and to identify the key factors required to accelerate the process, eight experts who play a crucial role in this socio-technical transformation were interviewed.

The analysis presented in this thesis aims to help understand the barriers and driving forces behind the adoption of PF as a critical component of a sustainable bioeconomy in the European Union. The insights gained from this research can serve as a foundation for policy and industry decisions, setting the course for an epoch of robust environmental resilience.

The subsequent chapters are organized as follows: Chapter 2 provides a literature review on the bioeconomy; the technology and application methods of PF to shape a bioeconomy; and recent research. Chapter 3 presents the methodology and research design, Chapter 4 discusses the findings from the expert interviews, and Chapter 5 discusses recommendations for future research, industry, and policy action.

2. Literature Review

2.1. The Vision(s) of a Bioeconomy

Visions of a bioeconomy are as diverse as the problems they are expected to solve. Therefore, the term '*bioeconomy*' is not universally defined and is widely diffused across various scientific fields and political strategies (Bugge et al., 2016). Around the globe, a wide range of actors, including governmental and non-governmental organizations, scientists, entrepreneurs, consultancies, and investors, are developing blueprints for what "the bioeconomy" will resemble (ibid.). These narratives consistently convey distinct perspectives on merging economy and ecology for economic development, with each vision having unique focuses and objectives (Vivien et al., 2019).

A literature review by Bugge et al. (2016) classified bioeconomy visions into three main types: *bio-resource*, *bio-technology*, and *bio-ecology*, as presented in Table 1. This classification was echoed by Vivien et al. (2019, Table 1) in their historical analysis of the bioeconomy term, which was first introduced in the 1920s. They particularly highlighted an emerging vision focused on industrial biotechnology as the driving force of the transition to a bioeconomy. The narrative around this vision was inspired by the progression of "traditional fermentation biotechnology to include genetic manipulation" (Bud, 1991 cited in Vivien et al., 2019) – a process known today as precision fermentation.

As this thesis examines the use of industrial biotechnology to achieve a bioeconomy, visions related to the bio-ecology vision can be set aside for the purpose of defining the bioeconomy within this context. Simultaneously, there is a clear focus on averting the exacerbation of our ecological crises and increasing EE. Consequently, sectors that cannot make a significant contribution to this goal are excluded from the scope of this thesis. Both the *bio-technology* and *bio-resource* visions place a strong emphasis on technology, natural sciences, and economic growth and thus overlap in parts (Bugge et al., 2016). Therefore, the focus of this thesis sits directly at the intersection: The vision of a bioeconomy being investigated here deals with the commercialization of advancements in industrial biotechnology (biomanufacturing), in this case, PF, to transformatively increase EE without compromising economic growth.

2.2. The (Microbial) Cell as the Factory of the Bioeconomy

Fermentation is one of the oldest technologies known to humankind (Ross et al., 2002). The term describes the process of the intentional use of microorganisms to metabolize organic matter into desired, simpler molecules (Ross et al., 2002). This fundamental technology has been a reliable companion to humans across the globe for thousands of years, and throughout history, technological advancements have enabled humans to develop increasingly diverse applications and products in food, beverages, pharmaceuticals, and beyond.

2.2.1. Microbial Fermentation: Humanity‘s Oldest Biotechnological Tool

The origins of fermentation can be traced back to early human civilizations. Fermented beverages have been found in the Henan province (today's China) dating back 9,000 years ago (McGovern et al., 2004), and initial cheese production dates back approximately 8,000 years to Mesopotamia (modern-day Iraq) (Ross et al., 2002). Even without understanding the underlying mechanisms, humans have harnessed the metabolic capabilities of microorganisms for various purposes, coinciding with the first domestication of plants and animals (Ross et al., 2002).

In 1676, Antoni van Leeuwenhoek made a groundbreaking discovery when he observed microorganisms under a microscope, revealing an unseen world of microscopic life (Dobell, 1932; Lane, 2015). This laid the foundation for future developments in fermentation and the understanding of the role of microorganisms in various biological processes. By 1857, Louis Pasteur revealed the role of microorganisms in fermentation, demonstrating that they were responsible for converting sugars into alcohol, carbon-dioxide (CO_2), and other byproducts. This finding led to the germ theory of fermentation and established microbiology as a distinct field (Barnett, 2003).

From the late 19th to the mid-20th century, industrial fermentation and biotechnology emerged as scientists and engineers harnessed microorganisms for large-scale applications (Demain & Adrio, 2008). This period saw innovations in the cultivation and optimization of microbial growth, which enabled the large-scale production of fermented products such as beer, wine, and other foods. Additionally, the discovery of aerobic fermentation during this time facilitated the production of compounds like citric acid (Papagianni, 2007) and antibiotics such as penicillin, discovered by Alexander Fleming in 1928 (Fleming, 1929).

Between the 1970s and 1990s, advancements in molecular biology, including the discovery of DNA's structure by James Watson and Francis Crick in 1953 and the development of genetic engineering techniques, revolutionized the manipulation of microorganisms for improved fermentation processes (Cohen et al., 1973). In 1973, Stanley Cohen, Herbert Boyer, and their colleagues developed recombinant DNA technology, which enabled the insertion of foreign genes into microorganisms, resulting in strains capable of synthesizing proteins not naturally produced by the host organism (Goeddel et al., 1979). This led to the commercial production of recombinant proteins, such as insulin and somatostatin (human growth hormone), using genetically engineered bacteria and yeasts (Walsh, 2005).

From the 1990s to the early 21st century, advances in molecular biology, genomics, and bioinformatics facilitated the development of metabolic and genetic engineering. Researchers began to modify and optimize entire metabolic pathways, rather than single genes, to enhance the production of desired compounds (Cameron et al., 2014). This marks the emergence of synthetic biology, which is paving the way for further advances in fermentation technology and enables humans to utilize microbes as 'cell factories' (Cameron et al., 2014). Subsequent chapters will provide a more detailed examination of *synthetic biology* and its influence on the development of fermentation processes.

2.2.2. Synthetic Biology: Unleashing New Potential for Fermentation

Synthetic biology is an umbrella term encompassing the application of engineering principles to the design and creation of novel biological systems using an interdisciplinary array of technological tools (Cheng & Lu, 2012; Flores Bueso & Tangney, 2017). These tools include the ever-evolving capabilities of metabolic engineering, which is facilitated by the advancements in genetic engineering, the understanding of metabolic pathways, and bioinformatics (Ko et al., 2020) – an interdisciplinary field that combines elements of biology with computer science and information technology (Luscombe et al., 2001).

Genetic engineering involves modifying an organism's existing characteristics or introducing new ones by directly manipulating its genetic material (Mutalik et al., 2013) and enables the conduct of metabolic engineering, the intentional redesign of a cell's metabolism to advance the production of native metabolites or enable the cell to produce novel products (Nielsen & Keasling, 2016).

Table 1: Visions and Narratives Around the Term "Bioeconomy"
(Source: Excerpt from Bugge et al. (2016) and Vivien et al. (2019))

Narratives according to (Vivien et al., 2019)

Name	*Type I bioeconomy*	*Type II bioeconomy*	*Type III bioeconomy*
Definition	An ecological economy, that is compatible with the biosphere	A science-based economy driven by industrial biotechnology	A biomass-based economy
Nature & Economy Relations	Struggle against entropy and co-evolution with the biosphere. Economic development in line with biological evolution	The cell is a factory Technology has the power to "correct God's mistakes"	Biomass replaces fossil fuels and mining to produce energy and materials

Visions according to Bugge et al. (2016)

Name	*bio-ecology vision*	*bio-technology vision*	*bio-resource vision*
Aims & Objectives	Sustainability, biodiversity, conservation of ecosystems, avoiding soil degradation	Economic growth & job creation	Economic growth & sustainability
Value Creation	Development of integrated production systems and high-quality products with territorial identity	Application of biotechnology, commercialization of research & technology	Conversion and upgrading of bio-resources (process oriented)

To achieve this, different methods such as recombinant gene expression, substrate[2] engineering, and protein engineering, can be used and combined (Ko et al., 2020). For the purpose of this thesis, it is not necessary to delve deeper into these methods, but to recognize that all these tools can be applied to modify, in the case of PF, the metabolism of microbes such as bacteria, filamentous fungi and yeasts, and algae (a) so that they produce desired products using desired substrates, and (b) to optimize this process in terms of scale and (economic) efficiency (Chai et al., 2022).

2.2.3. Precision Fermentation: Amplifying Synthetic Biology to Industrial Scale

According to Chai et al. (2022), the term '*precision fermentation*' emerged outside academia to describe the process of leveraging the synthetic biology toolkit for genetic and metabolic engineering of microbes, transforming them into '*microbial cell factories*' with the aim of efficiently producing desired molecules in an industrial setting. The term arose around the emergence of using metabolically engineered microorganisms to produce alternative proteins in food (The Good Food Institute, 2023), but is used more broadly in this thesis to describe engineered microorganisms that are used as factories in various contexts to convert carbon substrate (feedstocks) into desired (bio-)chemicals.

[2] A substrate, also known as a feedstock, is a molecule that is transformed by a chemical or biological reaction. In the context of fermentation by metabolically engineered microbes, it refers to carbon based raw materials (Lips, 2022).

PF brings the use of synthetic biology on microorganisms into an industrial setting. Consequently, to comprehend the commercial adoption of PF, it is essential to consider the entire production procedure, which goes beyond the mere utilization of synthetic biology tools in a lab setting. Hence, the initial configuration of the metabolic pathway is succeeded by strain optimizations aimed at enhancing the strain's economic efficiency and operational capabilities at larger scales:

At the beginning of the value chain is the selection of the target molecule and a strain that possesses the necessary characteristics for efficient production (Ko et al., 2020). Simultaneously, an appropriate feedstock is selected based on its availability, cost, and compatibility with the chosen microorganism - referred to as the strain (Ko et al., 2020). In constructing a scalable fermentation process for targeted molecule production, the utilization of the Design-Build-Test-Learn (DBTL) cycle, a core process of system design in synthetic biology, is a pivotal aspect. This cycle, characterized by its iterative feedback loop, facilitates strain optimization. The DBTL cycle is integral not only for the initial introduction of the capability to metabolize alternative substrates and to produce novel target molecules at a laboratory scale, but also for subsequent optimization of scale in terms of TRY – titer (end concentration of the targeted compound in the fermentation medium), rate (output per unit of time), and yield (quantity of the targeted synthesized per unit of raw material used) (Carbonell et al., 2018; Nielsen & Keasling, 2016).

The cycle involves four key steps:

1. **D**esign: A blueprint for the metabolic pathway through which the target molecule will be produced is de-

veloped, commonly involving the modification or introduction of genes into the strain that produce enzymes that facilitate the metabolic processes (Nielsen & Keasling, 2016).

2. **B**uild: This designed metabolic pathway is integrated into the strain. Applied here are advanced synthetic biology tools, including genetic engineering and bioinformatics, to improve the way the strain uses the starting material to produce the target molecule (Carbonell et al., 2018).

3. **T**est: The process performance is assessed. This examines the final concentration of the product in the fermentation environment, the quantity produced in a given time, and the efficiency of product generation per unit of feedstock used (TRY) (Carbonell et al., 2018).

4. **L**earn: The performance results of the test phase are incorporated into subsequent design improvements. If the performance is satisfactory, the process moves to the next stage. If not, the insights obtained from testing are used to modify the design (Carbonell et al., 2018).

The development of the initial strain variants takes place on a small scale within a laboratory setting. These are subsequently fine-tuned via iterations of the DBTL cycle, based on their anticipated performance metrics until they are ready to be transitioned to a larger fermentation unit. This process of scale-up involves an iterative optimization of the fermentation conditions, which is performed in conjunction with modifications to the metabolic pathways of the strains (Carbonell et al., 2018). The process takes place in progressively larger bioreactors, as per the model depicted in Figure 2 (Ko et al., 2020). Once the fermentation process concludes, target products are isolated from the rest of the fermentation broth through appropriate downstream processing techniques (Ko et al., 2020). With this approach, scientists, product developers, and engineers try to lift findings from the laboratory to an industrial scale with constant optimization on TRY.

2.3. Ways to Harness PF for Creating a Circular Bioeconomy

Chapter 2.1 presents a blueprint for a bioeconomy, wherein the EE of producing goods traditionally sourced from fossil fuels and animal origins is substantially enhanced via the deployment of biomanufacturing processes hinged on the metabolization of renewable feedstocks. As delineated in section 2.2, the application of metabolic engineering to microorganisms enables to turn them into 'microbial cell factories', utilizable to convert selected feedstocks into desired molecules such as chemicals, fuels, materials, and organic products (Ko et al., 2020, Figure 3). Therefore, this chapter aims to specify the potential role of PF, namely the large-scale utilization of 'microbial cell factories', in realizing the envisioned bioeconomy.

To produce the desired target molecules, microorganisms require a carbon-based substrate, often referred to as feedstock (Lips, 2022). In line with the defined vision of a bioeconomy, this discussion solely focuses on non-fossil-based feedstocks, which are categorized into three generations according to the chronology of their development and use:

1. First-generation feedstocks are derived from food crops that produce fermentable sugars. However, their usage has been associated with several undesirable environmental effects such as deforestation and competition for food supply, prompting the need for alternatives (Lips, 2022).

2. Second-generation feedstocks are sourced from lignocellulosic biomass, which includes energy crops and non-edible residues. As the most abundant renewable biomass, these feedstocks have the potential to reduce land usage and environmental impact. However, various forms of pre-treatment are required to convert them into a fermentable state (Lips, 2022; Morales et al., 2015; Soleymani Angili et al., 2021).

3. Third-generation feedstocks include brown macroalgae (Lips, 2022), and short-chain carbon-based molecules, including industrial waste gases like CO_2 and methane (Liu et al., 2020; Ruiz et al., 2023). Macroalgae, unlike first and second-generation biomass, grow in coastal waters, thus preserving arable land and freshwater, and do not require extensive pre-treatment for fermentation (Lips, 2022). The use of CO_2, the most widely available carbon source on Earth and methane, both GHG, would either prevent the emission of these gases into the atmosphere or bind them from the atmosphere (Venkata Mohan et al., 2016).

Currently, first-generation feedstocks form the backbone of resources used in these processes (Lips, 2022). However, developments in metabolic engineering and synthetic biology have significantly boosted the efficiency of microbial usage of feedstocks from the second and third generations, which are associated with wider availability, lower costs, and less negative impact on cropland use and the environment than the first generation (Lips, 2022; Pandey et al., 2021; Ruiz et al., 2023; Zhang et al., 2022). Notably, the use of industrial waste gases pivots the paradigm from a bioeconomy based on renewable feedstocks towards a circular bioeconomy (Venkata Mohan et al., 2016). In this model, emissions that would otherwise end up in the atmosphere are repurposed for the synthesis of food, cement, polymers, and chemicals (Ruiz et al., 2023).

In addition, synthetic biology offers significant potential for enhancing the sustainability of manufacturing processes not only at the input level, but also in improving the environmental impact of the resultant products. This can be accomplished through the integration of metabolic engineering with existing chemical processes (Ko et al., 2020) to yield bio-based products, or through the novel design and synthesis of entirely new molecules – *de novo* - with desirable characteristics (Keasling, 2010).

It is crucial to understand that many of the processes described here do not yet occur on a large scale but are an ag-

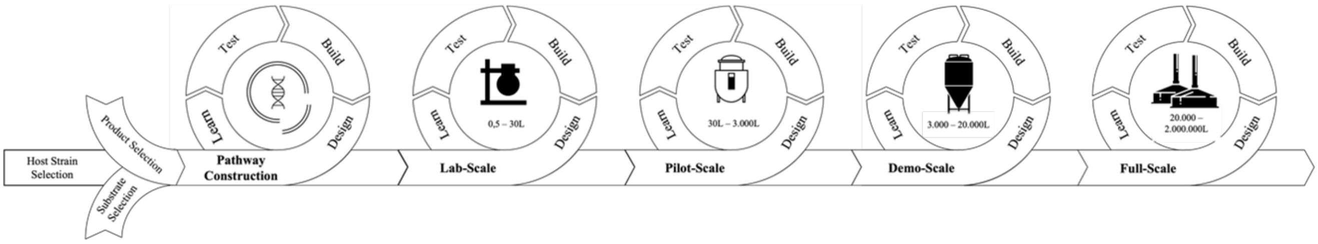

Figure 2: Employing the DBTL Cycle for Iterative Strain Optimization when Scaling Production (Source: Own illustration based on Carbonell et al. (2018) and Ko et al. (2020))

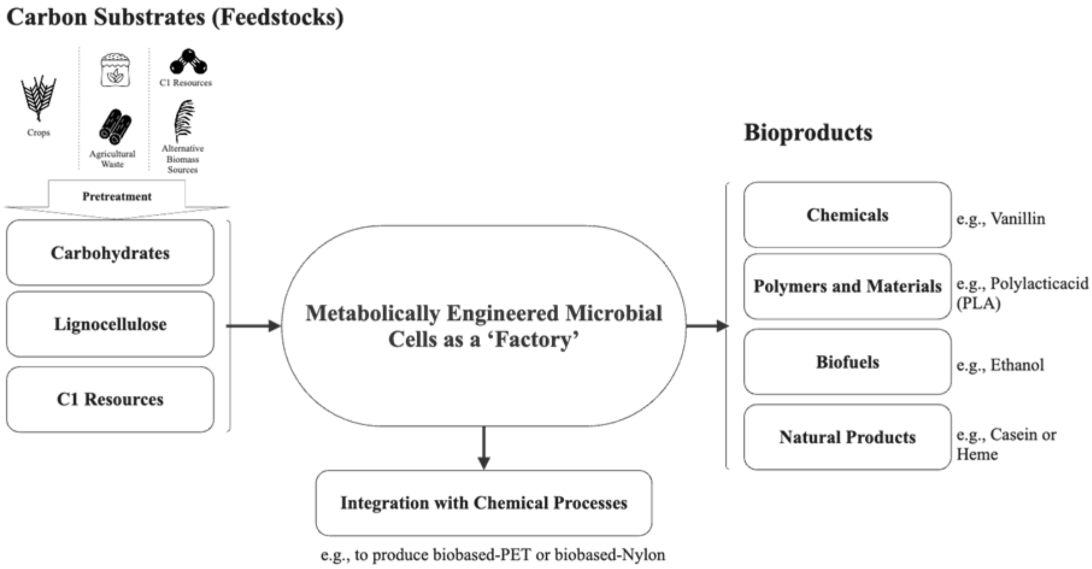

Figure 3: Using Metabolically Engineered Microbes as a Factory to Produce (Bio-) Chemicals from Various Carbon Substrates (Source: Adapted from Ko et al. (2020) and based on Liu et al. (2020))

gregation of successful laboratory experiments demonstrating the potential of the technology. For the envisioned bioeconomy to materialize, there's a need to raise these processes to commercial scales, optimizing both processes and strains to ensure market readiness. However, to facilitate this transition and successfully implement PF on a broad scale, understanding the various drivers and barriers influencing its adoption becomes a key factor. Consequently, the next segment of this thesis focuses on exploring these drivers and barriers, setting the stage for a detailed investigation into the dynamics that will shape the future of precision fermentation in the EU bioeconomy.

3. Methodology

3.1. Research Approach

This thesis aims to investigate strategies to accelerate the transition to a bioeconomy in the European Union, enabled by biomanufacturing, specifically PF. The research objective is the identification of principal drivers and challenges shaping current dynamics to then explore potential levers to accelerate the transition. Given the potential benefits of a bioeconomy driven by biomanufacturing, this thesis seeks to provide recommendations for policymakers and influential stakeholders to facilitate a potential transformation.

To address these objectives, the *Multi-Level-Perspective* framework, as conceptualized by Frank Geels (2002), is employed as an integrative conceptual lens for examining interactions between *macro*-, *meso*-, and *micro*-level processes within the EU that shape this transition. The MLP framework highlights the role of three interconnected analytical levels—landscape, regime, and niche—in understanding and shaping transitions. This framework is chosen for its ability to capture the complexity and dynamics of socio-technical transitions. The comprehensive scope of the framework to address the research question is further elaborated in Section 3.2.

Given the complex, broad research question, the scarcity of existing scientific literature, and the necessity for getting real-time insights into the potential ongoing transition, this study has chosen to utilize qualitative interviews as its principal data collection method. As part of this approach, eight carefully selected experts, each providing unique perspectives on the multi-faceted dynamics, were interviewed. The rationale behind choosing those experts is elaborated in Section 3.3, while the exploratory semi-structured questionnaire employed for the interviews is outlined in Section 3.4. Section 3.5 discusses the limitations of choosing this approach.

3.2. Taking a Multi-Level-Perspective on Technology Transitions

The potential adoption of PF as a transformative platform technology in the EU's main production sectors would imply a profound change in the way societal functions are fulfilled technologically, i.e., it implies a *technological transition* (TT) (Geels, 2002). According to Geels (2002), the trajectory of transformation research has shown that understanding these transitions requires a *socio-technical* perspective; an analytical lens that recognizes the intertwining of social and technical elements during the design, development, adoption, and use of technology. This perspective underscores that technology does not exist in a vacuum but is deeply embedded within its social context. It mirrors the values, interests, and power dynamics within the society in which it evolves Geels (2002). Using this lens also acknowledges the array of actors involved in technological transformations. These include not only the designers and developers of the technology, but also the customers and users, policymakers, and various other stakeholders. The interactions, negotiations, and dynamics among these diverse actors influence the direction and outcomes of the technological transformation (Geels, 2002).

Building upon this understanding of TTs as socio-technical phenomena, Frank Geels (2002) conceptualized the MLP framework. This framework has gained substantial prominence in elucidating technological societal transformations, particularly with respect to sustainability concerns (see Raven (2004) and Verbong and Geels (2007)). As it pertains to the exploration of drivers and barriers affecting the adoption of PF, employing the MLP framework provides a structured avenue for analyzing the complex dynamics influencing the potential transition within the European Union's manufacturing sectors.

The MLP framework distinguishes between three interrelated conceptual levels to analyze dynamics between actors: At the micro-level, *niches* act as incubators for radical innovation, protecting them in underperforming stadium from mainstream market selection (Kemp et al. (1998) as cited in Geels and Schot 2007). There, small networks of committed individuals interact to create momentum for their respective emerging technologies and practices that challenge the norms established at the meso level (Geels & Schot, 2007). This meso level, often referred to as the *socio-technical regime*, solidifies existing systems and outlines the path for dominant technological developments. It consists of a constellation of actors – among them corporations, policymakers, consumers, and markets – who manage and sustain the current socio-technical systems (Geels & Schot, 2007).

Micro and meso levels are subject to changes on the macro level, the *socio-technical landscape*. The macro level describes a broad sphere of exogenous influences that can be found, for example, in societal, macroeconomic, political, or environmental developments. These developments can influence the course and intensity of interactions between niche and regime by putting pressure on the established norms of the regime and thus creating spaces, so-called *windows of opportunity*, into which the niche can fall within the regime (Geels & Schot, 2007). The three levels form a nested hierarchy in which niches are embedded in regimes and regimes are embedded in the landscape (Figure 4).

Understanding the interplay between the different levels of the MLP framework is crucial for examining the drivers and barriers of a transformation process. Geels and Schot (2007) outline three core processes that facilitate the breakthrough of niche innovations into mainstream markets, where they compete with the existing regime:

(i) **Niche Accumulation**: Niche innovations gather internal momentum through learning processes, improvements in price/performance, and backing from influential groups.

(ii) **Landscape-Level Pressure**: Changes at the macro, or landscape, level exert pressure on the established regime.

(iii) **Regime Destabilization**: Destabilization of the regime creates windows of opportunity for niche innovations.

These processes, depicted in Figure 4, provide a foundation for examining the drivers and barriers of a potential technological transformation of the EU industry towards biomanufacturing via PF.

3.3. Interviewee Selection

For data collection, a meticulous selection of experts was carried out, and interviews were conducted with each of them, lasting between 30 and 70 minutes. Bearing the MLP framework in mind, these experts were chosen to represent different key pivot points within the framework, which allowed them to interact with various actors from the socio-technical regime or niche. A person is an expert, if she or he „has any responsibility for the design, implementation or control of a solution to a problem or [...] has privileged access to information about groups of people or decision-making processes" (Meuser & Nagel, 1991, p.443 (translated)). Concurrently, each interviewee possesses their own domain expertise and approaches the research question from their unique perspective. Table 2 offers an overview of the interviewees, including a brief introduction to the MLP framework. For a detailed list, please refer to Appendix A. Additionally, it was crucial to include experts with a life science background that bring an in-depth understanding of the technological aspects. Four of the interview partners have an academic life science background, with three of them holding a PhD.

In total, eight interviews were conducted. The interview partners were contacted via email. However, not all of the considered essential interviewees responded – primarily engineers and members of the established socio-technical regime, such as policymakers and representatives of industrial companies. Further details on this issue can be found in the limitations section.

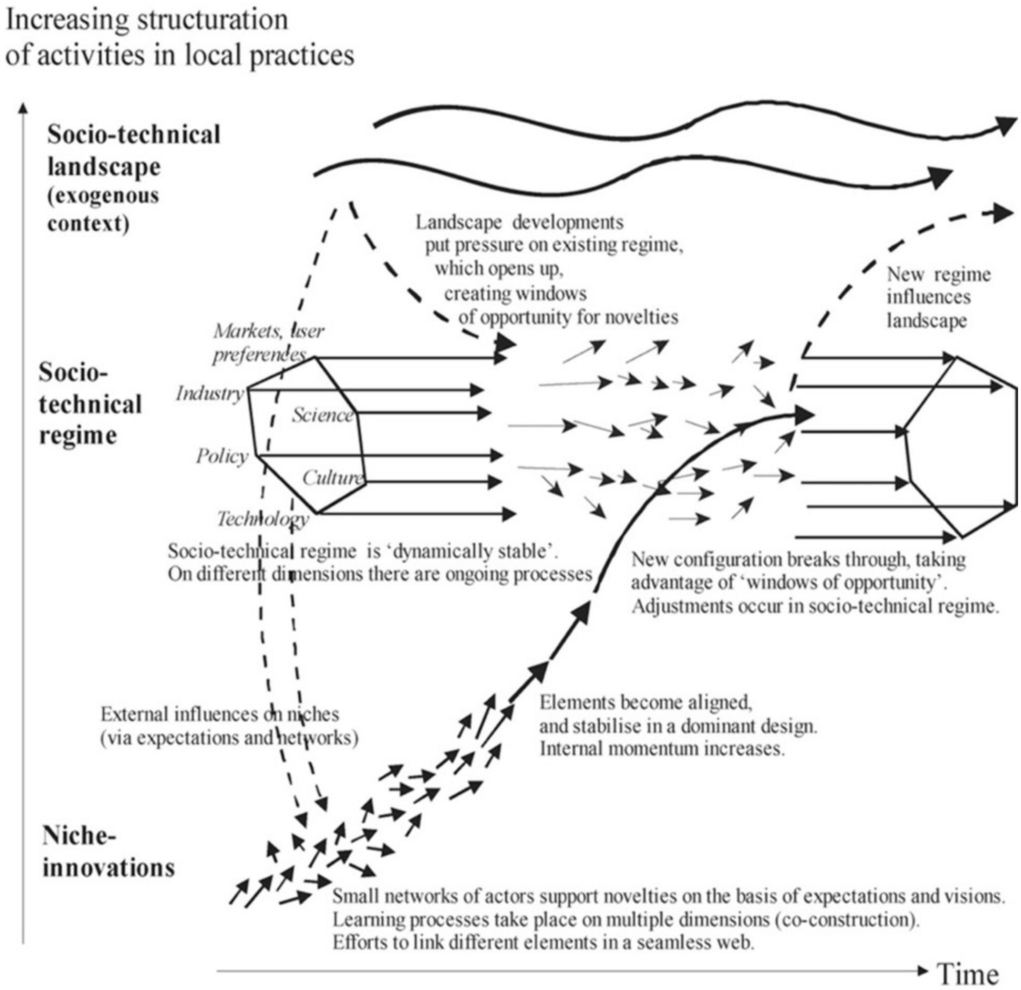

Figure 4: The Multi-Level Perspective on Transitions (Source: Geels and Schot (2007))

3.4. Questionnaire Structure

To maintain a balance between structure and flexibility in exploring the research questions, the interviews were conducted using a semi-structured, exploratory approach. This methodology allowed respondents to freely express their individual perspectives, impressions, and priorities within a clearly defined framework. The questionnaire was organized into five pre-formulated topical areas (see Table 3), which were shared with respondents several days ahead of the interview to allow for thoughtful preparation. The exploratory nature of this approach was designed to address the existing limitations in the researcher's knowledge and the scarce academic literature concerning metabolically engineered microbes as transformative societal technologies. It also provided the requisite flexibility to maintain an open perspective, facilitating the acquisition of new insights and the formulation of deeper probing questions.

3.5. Method of Analysis

The majority of interviews were conducted in English, although a few were carried out in German when interviewees felt more comfortable answering in their native language. The interview recordings were transcribed using the web tool *Trint*[3], and confidential company and personal information were anonymized. The transcripts may be provided upon request.

In the qualitative analysis, the thematic analysis method by Braun and Clarke (2012) was utilized. The MLP framework functioned as the overarching theoretical foundation, while specific themes and sub-themes emerged from the interview data, fitting within this framework for coding purposes. This approach, following Braun and Clarke (2012), enables the integration of both deductive and inductive reasoning. The ensuing flexibility allows for a systematic organization and assignment of themes and patterns throughout the interviews, thereby fostering the development of valuable insights within the structured context of the MLP framework while maintaining rigor and transparency. The analysis of the interviews was conducted in their respective spoken language using the analysis software *MAXQDA 2022*[4].

[3] www.trint.com is a web-based transcription software that can automatically convert video and audio files into transcripts.

[4] MAXQDA 2022 is a software for computer-assisted qualitative data and text analysis.

Table 2: Interview Partner Selection (Source: Own illustration)

No.	Function	Organization Type	Rationale for Inclusion
1	Management Consultant	Management Consultancy	Works with the niche and the socio-technical regime; unique perspective on landscape pressure on regime; and interactions between niche and (industry) regime.
2	Investment Manager	Venture Capitalist	Works from the niche with several PF companies, has a short- and long-term view on drivers and challenges of potential niche development.
3	Doctoral Student in Law, Consultant	University: Faculty of Life Sciences: Food, Nutrition and Health; Faculty of Law and Economics	Works with the established regime on interactions with the niche, especially from a regulatory perspective.
4	Scientist and Entrepreneur	Biotechnology Start-Up	As a core niche actor, the expert offers a micro-level perspective on developing and commercializing innovations from PF.
5	Policy Affairs Manager	Non-Governmental Organisation	Regularly collaborates with start-ups (niche), corporations, research institutions, and government bodies (socio-technical regime) to promote interactions.
6	Scientific Director and Investment Director	(Impact) Venture Capitalist	Takes a short-term and long-term perspective on the challenges and drivers of the niche's potential development, grounded by a deep technical and economic understanding. Facilitates interactions between the niche and the established regime.
7	Professor of Communication Studies and Author	University: Department of Communication Studies	Provides unique insights into the status, challenges, and opportunities faced by niche actors in communicating their vision to the regime; how the landscape pressures the socio-technical regime.
8	Researcher and Consultant	Private and Independent Research Institute on Renewable Carbon and Bio-Based Materials	Works with government institutions and industrial companies (socio-technical regime), start-ups and research and development (R&D) labs (niche); acts as observer and facilitator of multi-level interactions.

In accordance with the guidelines for thematic analysis provided by Braun and Clarke (2012) the first step after conducting and transcribing the interviews was to familiarize oneself with the data. This process entailed thoroughly reading and re-listening to the interviews, accompanied by note-taking on paper to highlight particularly insightful statements, patterns and commonalities across interviews.

In the following phase, an in-depth review of the theoretical foundations underlying the MLP framework was conducted. This review aimed to identify the drivers and barriers identified within the theory. In conjunction with this, both the recent updates to the framework and the foundational scientific research upon which the framework is based were examined. Notably, key literature from Kemp et al. (1998) and Geels and Schot (2007) provided significant insights. These explorations facilitated the creation of a deductive conceptual theme formation, which was used for the initial coding in the software.

Subsequently, bearing in mind the theoretical framework of the MLP and the derived codes, sub-themes were generated to which the identified categories could be assigned within the theoretical framework. This stage involved an iterative process of theme refinement, during which themes were discarded, added, merged, subdivided, or renamed as they emerged, ensuring a comprehensive and robust analysis under constant reflection with regard to conciseness and relation to the question. The final coding can be found in Appendix B.

4. Results

By their very nature, explanations of socio-technological transition reflect the interrelation and complexity of the dynamics within the conceptual levels. In order to account for this complexity and simultaneously present structured analysis findings, the following chapters are formulated around

Table 3: Brief Interview Guideline (Source: Own Illustration)

No.	Subject	Rationale
1	Diving deeper into the expert's background and touchpoints with bioeconomy and PF	Discovering further information and touchpoints with the research question that are not publicly available.
2	Vision of a realized bioeconomy	Gaining insights into the interviewee's unique perspective on the vision of a bioeconomy; the role PF may play in it; opinion on the feasibility of a transition and the status quo.
3	Mapping challenges and obstacles of PF	Exploring the obstacles and challenges that are concretely relevant to the domain of the expert or from the perspective of the expert for a widespread adoption of PF, i.e., the challenges faced by the niche when attempting to (broadly) participate in the socio-technical regime.
4	Mapping catalysts and facilitators of PF	Exploring the catalysts and facilitators the expert perceives concretely in their domain or from their expert or from the perspective of the expert for a widespread adoption of PF, i.e. (potential) dynamics that spur the niche-actors to strengthen their position in the socio-technical regime.
5	Deriving an action plan	Initiating a constructive discussion on the possible actions that influential actors in the EU can implement to accelerate the transition to a bioeconomy by driving the adoption of PF.

the three core processes of a socio-technical transition according to (Geels & Schot, 2007): (i) niche accumulation, (ii) landscape-level pressure on the regime, and (iii) destabilization of the regime. These processes are supplemented with barriers and drivers delineated by (Geels, 2002), which build upon the foundational research in strategic niche management by (Kemp et al., 1998) and the challenges of niche-regime interactions due to lock-in effects, as described by (Unruh, 2000).

The interviews reveal that the niche mainly consists of start-up companies conducting their own R&D and striving to commercialize their technology. Universities and research institutions also play a role, but often there is a lack of practical transfer. Occasionally, large corporations also initiate and establish business units that can be associated with the niche. However, the majority form part of the socio-technological regime that maintains current industrial structures and responds to existing market and user preferences, while simultaneously shaping them.

Furthermore, in the case of PF, the regulatory, political, and legal dimensions emerge as one of the key actors in the socio-technical regime. The European Commission (EC), along with the regulatory body and governments of individual nations, set the stage for innovation, approval, and market distortions. They are all subject to the changes and influences on the landscape, which in the context of PF adoption, particularly manifest when they threaten the current structures and norms of the regulators and industry, as well as influence market and user preferences.

Section 4.1 of the results focuses on niche progression in terms of (i) niche accumulation. It discusses the drivers of this accumulation, including learning effects, improvements in cost-efficiency, and the involvement of influential stakeholders such as venture capitalists, corporate venture capitalists, partnerships between incumbent companies and niche players, and new business units dedicated to the niche. Concurrently, it explores barriers, as per Kemp et al. (1998) and Geels (2005), such as technological challenges, infrastructural gaps, and difficulties in integrating relevant factors into a cohesive European entrepreneurial ecosystem.

Section 4.2 delves deeper into the challenges faced by the niche when interacting with the socio-technical regime. It explores the impact of regulatory frameworks, cultural and psychological factors, price lock-in, mismatches and other external impediments to niche growth.

Section 4.3 turns its attention to how landscape shifts – both long-term sustainability issues and short-term factors like the need for resilient supply chains in light of pandemics, European military conflicts, and escalating geopolitical tensions – exert additional pressure on the existing socio-technical regime. Consequently, parts of the previously closed regime, discussed in 4.2, begin to open up, offering opportunities for the niche.

Thus, the structure of the results section uses the concepts and dynamics of a technology camouflage of the MLP framework to describe drivers and barriers. At the same time, however, it is not intended to present the entire framework or the concrete processes, but rather to use them to help answer the research question, namely the question of the most influential drivers and barriers on the path to PF. According to the methodology and the research question, not every actual driver and barrier is named or described in detail. Only a selected part emerges from the interviews, but at the same time one or more of the experts consider them to be the most relevant.

4.1. Niche-Accumulation

Geels and Schot (2007) propose a theoretical model where niche accumulation gains momentum through three key components: learning processes, improvements in the price-to-performance ratio, and the involvement of influential entities supporting the process. In the case of PF adoption, these processes turn out to be interlinked: Technological advancements are notably driving improvements in the price-performance ratio in research and development, and in scaling up processes. These enhancements raise the likelihood of successful penetration into new niches. Consequently, this progress piques the interest of influential stakeholders, including investors and established industry players. Such entities, anticipating transformative shifts or eyeing new market entry, are inclined to invest further in research and development to align the technology more closely with market demands.

The interplay of these factors has so far contributed to significant progress in the realization of envisioned applications of the technology, so that a variety of novel processes have been presented and tested at lab-scale. At the same time, the interviews reveal that although significant strides have been made, there is still much ground to cover to overcome niche internal barriers to close the gap between lab-scale research and commercialization, manifested in the need for further scientific knowledge, funding and entrepreneurial talent, and availability of fermentation capacity and feedstocks.

4.1.1. Learning Curve Effects in Technology and Commerce

Driver I: DBTL-Acceleration Driving Innovation Capabilities

Based on the interviews conducted, it's evident that significant strides in synthetic biology have greatly driven the advancement and commercial viability of PF technology. As described in Chapter 2.2, the progression of PF is intrinsically tied to the enhancements in synthetic biology and biomanufacturing, which have made it possible to scale these synthetic biology processes industrially. The resources, speed, and capabilities required for the initial processing and optimization of strains within the DBTL cycle heavily depend on the knowledge available and the performance of the tools at hand.

The interviews identified four central technological advancements contributing to the niche accumulation we see today:

1. the continued improvement of synthetic biology tools (Expert 1, Pos. 7, Expert 4, Pos. 5);
2. the standardization and operationalization of these tools, extending their use beyond the initial inventors (Expert 1, Pos. 13);
3. a deeper understanding of the refinements necessary for process scaling (Expert 2, Pos. 11; Expert 4, Pos. 5);
4. the development of cost-effective strategies for R&D, upstream and downstream processing (Expert 2, Pos. 11; Expert 4, Pos. 5; Expert 8, Pos. 25).

The impact of these technological advancements has broadened the technology's applicability, enabling more individuals to conduct an increasing number of experiments with less resource requirement. This advancement has also multiplied the possibilities of strain optimization, increasing the speed and effectiveness of experiments.

These technological advancements enabled a wide array of research initiatives undertaken by universities, start-ups, and industrial research departments. The progress achieved through these projects underscores the potential of medium-scale biomanufacturing, drawing attention to the trajectory of this technology within its niche. This trajectory is attracting an increasing number of entrepreneurs, scientists, investors, and members from established industry regimes. (Expert 2, Pos. 33; 39) They anticipate that the ongoing improvements in these areas will continue to propel PF forward, extending its range of applications (Expert 2, Pos. 19). As such, the interviews make it clear that this expanding technological trajectory, now accessible to a broader audience, is a major driver of niche accumulation and is expected to remain so in the future.

Driver II: Entrepreneurs Evolving Through Commercial Acumen

For the commercialization of the technological advances, it is crucial to recognize that the development of business acumen by entrepreneurs in the niche is essential. Even when windows of opportunity arise through landscape changes, as described in the forthcoming chapters, it does not mean that niche technology simply falls into place. Niche actors must a) be technologically capable, and b) recognize the possibility of seizing those windows. This overlaps with the core ideas of strategic niche management, in which it is asserted that markets do not merely exist but are actively created and shaped by the strategic actions of niche actors, reflecting their visions, learning processes, and networks (Kemp et al., 1998).

Taking the example of *LanzaTech*, Expert 8 (Pos. 25) describes how the company initially struggled against the price lock-in (Chapter 4.2.3) of the commodity markets for fuels and plastics. Only after the predominantly scientific team hired a commercial executive did they expand their focus to markets where the CO_2 recycled ethanol from PF already found acceptance today due to its sustainability aspects, despite a price premium. (Expert 8, Pos. 25). They then began collaborating with Unilever, L'Oreal, and other direct-to-consumer brands whose customers were willing to pay the necessary price premium for perceived increased environmental friendliness (Expert 8, Pos. 25).

Furthermore, Expert 4 describes how niche actors have learned to navigate the challenges of internal resistance within established companies when introducing innovative products that could potentially cannibalize existing business (Expert 4, Pos. 29). They have found success in partnering with companies without current market access that can benefit from the niche actor's technology to enter new markets (Expert 4, Pos. 29). The windows of opportunity that therefore potentially open for niche entrepreneurs are discussed in Chapter 4.3.1.

Niche actors have recognized the importance of conducting market research early on and identifying the parameters for the product that will break the market (Expert 4, Pos. 5). They have also learned to choose markets with fast innovation cycles, enabling them to gain credibility and scale quickly (Expert 4, Pos. 5). Additionally, niche actors have focused on selecting product classes with sufficient knowledge, interest, and product-market fit from the outset (Expert 4, Pos. 5). All this contributes to the fact that niche technologies manage to conquer markets and thus drives niche accumulation, and ultimately the adoption of PF.

Barrier I: Technological Limitations

However, PFs have only been able to establish themselves in a few very high-priced niches that entered because they solved problems internal to the established regime (Expert 2, Pos. 33). Although technological advancements are recognized as one of the primary drivers of the niche, the interviews also underscore that the current limitations of the technology represent significant barriers to further penetration of the niche into additional markets.

As Expert 2 (Pos. 23) emphasizes, performance on the TRY indicators is key for economic viability. For this, further optimization of the price-performance metrics of the large-scale production processes is necessary in many niches, the implementation of which is primarily hindered by previously impossible strain optimization along process scale-up.

Currently, the implementation of these improvements is largely hindered by insufficient strain optimization, largely due to a lack of understanding of the causal relationships between specific genetic mutations and their effects on yields (Expert 1, Pos. 7). The vast number of potential permutations of genetic modifications adds to this complexity, making it challenging to identify combinations leading to optimal results (Expert 1, Pos. 9) and translating progress in the lab into larger scales (Expert 8, Pos. 11).

The large-scale production mainly utilizes a few well-studied, 'brute-force' legacy strains (Expert 6, Pos. 11), whose optimization potential has largely been exhausted (Expert 2, Pos. 11). However, expanding to other organisms is also faced by several challenges, as genetic tooling for non-model organisms, such as fungi and algae, is a slow process that can take 5-10 years (Expert 1, Pos. 7). And even when a novel organism has been prepared for the first large-scale productions, these often do not take place because the Contract Manufacturing Organizations (CMOs) to which start-ups outsource their fermentations are not used to them, or they have not yet gained the trust of authorities or customers (Expert 4, Pos. 5).

4.1.2. Driver III: Ecosystem Emergence Around the Niche

As detailed in the preceding chapter, technological advancements have increasingly brought potential applications into focus. This enhanced visibility has piqued the interest of venture capitalists and well-established industry players, identifiable in the MLP as the involvement of influential actors (Geels, 2002). These entities now engage with the niche, aiming to participate in the potential commercial success and threat to current value chains it represents. In addition to their vested interest, they offer essential support to the niche through financing, infrastructure and distribution networks, and a comprehensive understanding of the market dynamics to niche actors.

Venture Capitalists

VC involvement is a critical driver contributing to niche accumulation at multiple levels (Expert 2, Pos. 19; Expert 5, Pos. 28; Expert 6, Pos. 19). Through their early-stage, high-risk investments in start-ups, VCs help bridge the gap between basic research and commercialization by providing the funding and support necessary in hope to turn scientific discoveries into viable and scalable businesses (Expert 2, Pos. 19).

By nature, VCs focus on funding promising young companies that display high growth potential and a chance to become important players within the industry regime, motivated by securing substantial returns on their investments. Therefore, their contribution to niche momentum extends beyond financial support, as such investments form well-established VC funds have significant signaling effects on the potential trajectory of PF to actors outside the regime – especially in the case of PF where the experts highlight that the total invested capital increases, and the number of funds interested in the application of the technology grows (Expert 2, Pos. 21; Expert 5, Pos. 28). This is further accelerated by the trend of increased VC investor awareness regarding sustainability metrics (Expert 6, Pos. 19; Expert 4, Pos. 7). This validation attracts further young scientists and entrepreneurs to explore venture building opportunities in the space (Expert 2, Pos. 19).

Furthermore, the intersection of biology and information systems has further broadened the investor pool, attracting those beyond traditional industry boundaries as showcased by the entrepreneurial journey of Expert 4 (Pos. 3), whose start-up emerged from an artificial intelligence venture studio[5].

[5] A venture studio is a company that systemically builds start-ups by incubating own ideas (Blank, 2022).

Corporate Engagement

Additionally, the involvement of established companies from the industry regime drives niche accumulation through joint ventures, product collaborations, investments via Corporate Venture Capital (CVC) (Expert 5, Pos. 46), or the creation of their own R&D units focused on PF. The participation of the established regime actors enables the niche access to market understanding, infrastructure, resources, and distribution structures that were previously not as accessible. This interaction not only increases the visibility and legitimacy of the niche but also enhances its capacity to penetrate and transform the prevailing socio-technical regime.

An example of how established companies proactively anticipate and facilitate change within their value streams is the German company *InFamily Foods Holding GmbH & Co. KG*. Following the 2020 merger of two traditional German butchers, *H. & E. Reinert Westfälische Privat-Fleischerei GmbH* (founded 1931) and *H. Kemper GmbH & Co. KG* (founded 1888), the company has restructured its operations. It now sees a future for protein production based on three pillars, incorporated in three subsidies: conventional animal production (*The Family Butchers GmbH*), plant-based imitates of animal protein sources (*The Plantly Butchers GmbH*), and cellular precision agriculture including PF (*The Cultivated B GmbH*) (Expert 5, Pos. 46; InFamily Foods (n.d.)).

In this context, it is evident that some incumbent companies have started to counterbalance the incremental innovation of the entrenched socio-technical regime by fostering niches. This action signifies a degree of openness towards the niche, and consequently towards alternatives to the patterns of the established regime. Nevertheless, the interviews revealed a number of barriers within the EU entrepreneurial ecosystem that contribute to the fact that niche innovations often fail to make the leap to commercialization.

4.1.3. Market Transition Hurdles for Niche Innovations

Despite the strong momentum in the niche, only a fraction of laboratory innovations makes their way into commercial applications. The barriers to this transition are numerous: beginning with the challenge of bridging the gap between research and practice, niche actors striving to translate their technology into a market-ready state encounter obstacles related to financing, availability of infrastructure, product approval processes, and the difficulty of achieving a suitable product-market fit.

Barrier II: Lack of Guidance in Spinning-Out University Research

Expert 1 (Pos. 17) underlines the lack of entrepreneurial mandates of many universities within the EU. Many research institutions within the EU conduct relevant research that could advance the technology trajectory of PF and increase market viability, but with few exceptions, they have no relation to the transfer of this into practice. Expert 6 (Pos. 15) and Expert 4 (Pos. 41) share the same opinion and praise the research efforts of the EU, but equally point out that those laboratory innovations are not shown a way into application.

Furthermore, it is shown that even if technology ventures into the niche in the form of a spin-out[6], scaling up PF technologies and building infrastructure requires operational and manufacturing expertise, which is often not found in young university founders (Expert 6, Pos. 15). This results in a further reason PF start-ups may struggle to close the gap between initial research and commercial application.

The Valley of Death[7] on the Horizon

However, actual lack of guidance in value creation is not a problem exclusive to university founder. Expert 5 describes the current situation of entrepreneurial niche players, especially start-ups that are dependent on VCs backing, run the risk of sinking into the so-called *Valley of Death* in the current market environment, i.e., failing as a result of failing to successfully commercialize (Expert 5, Pos. 34; see Figure 5).

The threat of a fall into the *Valley of Death* for entrepreneurial niche players is an interplay of several unfavorable factors, and differs slightly from start-up to start-up by segment and product type:

a) A significant proportion of start-ups struggle with the limitations inherent in optimizing traditional strains and incorporating novel strains when scaling up their fermentation process (as detailed in 4.1.1).

b) Many start-ups face a volatile investment environment, reliance on US investors, and a conservative stance from EU investors when attempting to secure follow-on investments for the scaling and commercialization of their technology (as discussed in 4.1.2).

c) Those start-ups focused on designing specialty molecules to solve existing material and chemical manufacturing issues often miss the mark in terms of product-market fit. They struggle to identify the real pain points of their potential customers, which could guide their resource use (as outlined in 4.1.2).

d) Companies using PF to produce novel foods have to navigate a costly, and uncertain approval process in the EU before they can market their product. So far, no company has successfully received approval for a novel food produced by PF in the EU (as described in 4.2.1).

e) Particularly for companies aiming at large-scale production, such as those in the food, chemicals, and ma-

[6] A spin-out is a newly founded company that is co-founded by a university or research laboratory, which owns the licensed technology and applies it to the market with the aim to leverage available academic knowledge for commercialization (Clarysse et al., 2011).

[7] The Valley of Death is a metaphor used to describe the gap that exists between the research and development of new technologies or products, and their successful commercialization or implementation (Auerswald & Branscomb, 2003).

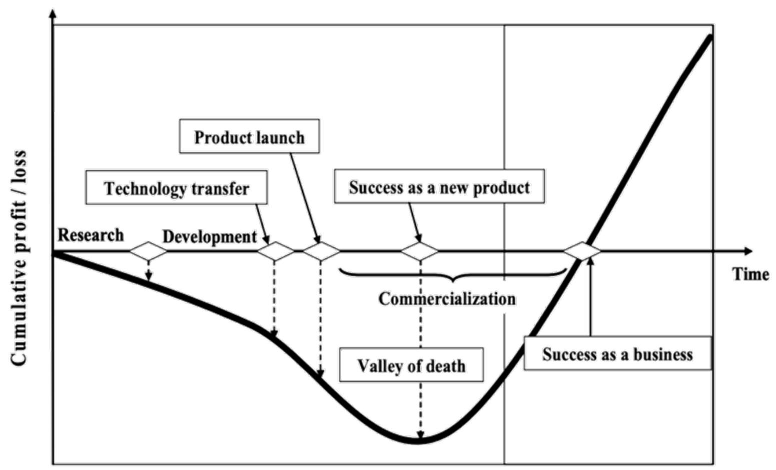

Figure 5: The Failure of Start-Ups Due to Inadequate Value Creation from their First Products is often referred to as the 'Valley of Death' (Source: Osawa and Miyazaki (2006))

terials sectors, there is a perceived lack of sufficient fermentation capacity to carry out their production within the EU (explained further in 4.1.2).

The interrelationships between the factors that lead to commercialization challenges and thus to the potential demise of PF start-ups in the EU differ from company to company but are often intertwined. Start-ups whose product approval is uncertain or who do not know which use case to put their current and future resources into are also more difficult to obtain funding in an already volatile investment environment. Start-ups that do not receive funding also do not find opportunities to expand their technical and infrastructural capabilities.

Barrier III: Lack of Commercial Insights to Create Value from Technological Novelty

Expert 4 describes the difficulties he and his peers, other biotechnology entrepreneurs, face when trying to develop suitable products with potential customers from large corporate chemistry: Many of these customers cannot or will not disclose their problems.

> *"[one would think], the question [...]: 'Hey, have you got any problems that I can help you solve [. . .]?' would be a pretty open-ended question and that you get answers pretty quickly. It's probably one of the worst questions you can ask in innovation because those problems are almost more valuable than potential solutions. [The potential industry customers], they know the problems that their end customers have and they're trying to solve them with their internal technology and that information is more valuable than anything else. Because again, the main problem of biotech companies [...] seems to be they're trying to solve problems, but they don't have good access to the problems because they don't have the market positioning" (Expert 4, Pos. 29).*

Expert 1 (Pos. 17) confirms this problem, telling from his consulting work with some of the largest material corporations in the world: *"there's a big knowledge gap. Obviously, industries and big players, they keep the secrets about their formulations, they don't reveal everything. And so [...] as a start-up, [you] don't actually know what's the pain point."*

The viewpoints of the entrepreneur operating within the niche and the strategy consultant working with large corporations provide intriguing perspectives on a shared issue: A communication gap exists between major customers attempting to address regime intrinsic problems and niche actors seeking guidance to identify pain-points and establish product-market fit. This gap constitutes a barrier to the adoption of PF as it curtails the niche's momentum and preserves the socio-technical regime.

Barrier IV: Volatile Funding Environment

As touched upon earlier in the discussion of factors contributing to a potential valley of death for PF start-ups, several experts interviewed make it clear that the VC funding environment is difficult to secure for subsequent investment rounds (Expert 4, Pos. 41; Expert 6, Pos. 15). These investments, typically a Series A round, are characterized by capital to be used for market entry. As the listed difficulties show, many start-ups are not clear on how to venture to commercialize their technology and thus enter the market (Expert 1, Pos. 17).

Raising a follow-on investment round generally appears to be more difficult for VC funds within the EU due to their reputation for being more risk-averse than their U.S. counterparts (Expert 4, Pos. 41; Expert 6, Pos. 15). This creates a dependence on U.S. investors among European companies, whose presence can never be relied upon due to exogenous factors (Expert 4, Pos. 41). Moreover, economic volatility exacerbates these financing problems, as Expert 6 (Pos. 15) points out. EU Investors' risk aversion will become all the more relevant, especially in the coming sub-chapter with regard to financing fermentation plants.

Barrier V: Lack of Infrastructure for Commercial Scaling

The lack of availability of fermentation capacity, particularly in the form of bioreactors for production beyond the lab-scale, is further contributing to this bundle of challenges (Expert 1, Pos. 7; Expert 5, Pos. 32; Expert 8, Pos. 31). Start-ups, primarily those pre-revenue and backed by venture capital, oftentimes lack the financial means to build their own capacity for large-scale fermentation. Simultaneously, the experts raise the concern about the lack of CMOs within the EU to facilitate large-scale production for these start-ups (Expert 6, Expert 2, Source).

This infrastructure bottleneck hinders start-ups, particularly those that a) lack their own fermentation facilities and b) need to achieve economies of scale to compete with inexpensive commodity products (Expert 8, Pos. 25). Having no fermentation capacity available prevents them from replicating lab results at larger scales, illustrated by the experiences of start-ups producing staple foods or chemicals for fuels and plastics using PF (Expert 6, Pos. 5; Expert 8, Pos. 11; Expert 1, Pos. 9). On the other hand, Expert 4, who operates in the premium cosmetic ingredients sector, does not view this as an immediate concern but recognizes the limitations imposed by CMOs regarding the use of specific strains (Pos. 5).

Securing financing for such infrastructural investments presents a significant challenge as neither equity investors nor lenders are ready to provide capital. Experts 1 (Pos. 7), 2 (Pos. 7), 4 (Pos. 23), and 5 (Pos. 34) clarify that neither VCs nor traditional banking institutions are eager to bear the risk associated with financing a fermentation plant (Source). For VCs, the investment required, often in the high million Euro range, far exceeds their typical investment thresholds. Banks, on the other hand, view the risk of financing infrastructures for start-ups as carrying an unacceptably high risk of default.

As a result, many start-ups remain trapped in the lab-scale test phases of their strain optimization processes, unable to either refine their production processes or demonstrate their potential to prospective partners and customers (Expert 1, Pos. 7). Expert 1 (Pos. 9) provides an apt illustration of this issue, noting,

> *„So, a lot of, let's say, the good ideas of start-ups, they don't even make it to commercial scale. And then if they make it, if they have proven it, then basically a big international player still can't do anything with them because there's no manufacturing capacity available[. . .]."*

The infrastructure and financing gap outlined above thus poses significant challenges that need to be overcome to enable these start-ups to produce on a large scale, slows down niches from expanding and professionalizing, and thus poses a barrier to niche accumulation and thus adoption of precision fermentation, especially in the commodity manufacturing sector.

4.2. Ways of Regime Lock-In – Barriers to Niche Momentum

After examining niche internal drivers and barriers in 4.1, this chapter focuses exclusively on the barriers that cause niche impulses to fail at the gates of the established regime.

4.2.1. Barrier VI: Regulatory Framework for Novel Foods[8]

The regulatory framework in the EU, as well as the decision-making structure, is a hurdle frequently mentioned by the experts for the market entry of novel foods from PF (Expert 2, Pos. 13; Expert 3, Pos. 21; Expert 5, Pos. 34; Expert 6, Pos. 29). These barriers are characterized by the duration, complexity, and lack of guidance in the approval process for novel foods, the uncertainty surrounding final authorization outcomes, and coordination challenges among EU Decision-making institutions.

The European Food Safety Authority (EFSA) has been identified as a key player in the slow and inefficient authorization processes for novel foods using PF technologies, embedded in the bureaucratic and unpredictable construct of the EC (Expert 2, Pos. 13; Expert 3, Pos. 21). The approval process usually takes around two years. However, the actual duration can differ significantly depending on the level of detail required, additional data requests, and the bureaucracy surrounding the EFSA's guidelines and decision-making procedures (Expert 3, Pos. 21). Furthermore, the EFSA's divergence from its guidelines has created regulatory uncertainty, complicating the regulatory landscape for PF companies (Expert 3, Pos. 21).

The uncertainty surrounding the appropriate regulatory classification of PF products has added to the challenges faced by companies in this sector (Expert 3, Pos. 27). PF companies trying to enter the EU market have chosen to register their products as Novel Foods or as foods containing genetically modified organisms (GMO)[9]. Expert 3 (Pos. 27), a legal scholar surveying these processes, cannot say either which process should be the preferred choice of niche actors; the EU does not provide any guidelines, and so far none of the companies has successfully obtained approval. This ambiguity and lack of guidance leads to uncertainty, high

[8] A novel food is defined as a food that had not been consumed to a significant degree by humans in the EU before 15 May 1997. This can include foods that are newly developed, innovative food, food produced using new technologies and production processes, as well as food which is or has been traditionally consumed outside the EU. (European Commission, n.d.-b)

[9] Metabolically engineered microbes fall under GMOs in the EU because their genetic material has been actively modified. Products made from GMOs or produced by GMOs, as in the case of PF, are labeled as "genetically modified (GM) food or feed". They cannot be marketed in the EU without approval. (European Commission, n.d.-a)

costs, and lengthy approval processes, making market entry success slower and less likely (Expert 3, Pos. 27).

The complex decision-making structure of the EU entails coordination among multiple director generals and significant bureaucracy (Expert 3, Pos. 54, 55, 57). This bureaucratic structure impedes the progression of legislative proposals related to the sustainable food system package that could potentially benefit the PF industry (Expert 3, Pos. 31).

Despite the EU's aim to maintain both high consumer protection levels and foster innovation, striking the right balance has proven difficult (Expert 3, Pos. 55). Seeking the approval of the Commission and a majority of member states, even after products have been deemed safe by the EFSA, lends an added layer of uncertainty to the process (Expert 5, Pos. 34). Political landscapes further influence the final authorization outcomes (Expert 5, Pos. 34).

Given these regulatory challenges, start-ups in the PF sector have expressed concerns about operating within the EU (Expert 5, Pos. 34). The lengthy, bureaucratic, and uncertain approval process has led companies to consider other jurisdictions, such as the USA and Singapore, where regulatory environments are perceived as more supportive and efficient (Expert 5, Pos. 34). Consequently, investors are more likely to fund companies targeting markets with streamlined approval processes (Expert 5, Pos. 34).

Expert perspectives highlight that the present configuration of the EFSA and the broader framework of regulatory decisions at the EC level pose substantial barriers to market entry for niche food products in the EU. There is further concern about the potential exodus of companies, talent, and investors to foreign markets where these entities receive active government funding, regulatory guidance, and support for market entry (Expert 5, Pos. 34).

4.2.2. Barrier VII: Psychological and Cultural Factors

Even products are able to enter the market, the question after acceptance by decision-makers and consumers remains. The experts point out that the PF technology and products have received little attention so far. When decision-makers and consumers are confronted with them, there is skepticism about the use of genetic engineering.

Negative Perception of Genetically Modified Organisms

Negative perception and public distrust in GMOs were identified as a driver against consumer adoption of genetically modified products (Experts 1, 2, 3 & 7). Expert 1 (Pos. 15) and Expert 2 (Pos. 13) indicate that the public misunderstands GMO products, especially when they are presented in food products. GMOs that are used regularly for medicine, are "demonized" by media, and this is harmful to mostly unproblematic products.

Politicians reflect the negative perception of GMOs, as they are refusing to pass bills on the topic. According to Expert 3, Germany, for instance, chooses to abstain from voting when discussed in the European Commission. Germany's role may lead to the abstinence of other countries as well (Expert 3, Pos. 61).

Experts acknowledge that concerns regarding safety and the use of GMOs are fundamentally valid, demonstrating an understanding for possible apprehensions among individuals unfamiliar with the topic (Expert 7, Pos. 50). However, the extent to which these questioning transitions into excessive polemics and becomes a tool for groups aiming to disadvantage PF in favor of established processes, could pose a barrier to the establishment of an objective debate. This could further impede the advancement of PF products at both consumer and governmental levels in the food sector. (Expert 7, Pos. 50) This barrier is particularly relevant in the context of novel foods derived from PF, since, for instance, established food-technical products such as rennet, pharmaceutical products like insulin from PF, ethanol from PF, or human-skin identical collagen from PF face no significant consumer rejection or concerns. (Expert 2, Pos. 13; Expert 4; Pos. 9)

Cultural Aspects

Expert 3 underscores potential socio-political barriers to the advancement of foods produced through precision fermentation, citing Italy and France as representative cases (Pos. 57). Both countries symbolize societies deeply intertwined with their cultural heritage and identity through food and its origins. Experts 3 (Pos. 57) and 5 (Pos. 34) describe how Italy's government recently preemptively prohibited the marketing of cell-cultured meat, a product belonging to the cellular agriculture sector, allegedly to safeguard traditional food production and the agricultural sector.

Even if the ultimate products sold to consumers share the same molecular structure, Expert 5 emphasizes (Pos. 40) that the method of production plays a significant role:

"The milk does not come from the cow. That is already the problem. [translated]".

As nations heavily rooted in agriculture, most EU countries maintain a different relationship with the agricultural sector compared to import nations like Singapore and Israel, which are further advanced in the authorization of PF products (Expert 5, Pos. 40).

A shift toward food from bioreactors may be perceived as unsolidary with small-scale farmers. A fallacy, according to Expert 7 (Pos. 64), a Professor of Communication Studies specializing in agricultural systems, comparing the developments in the EU to observations from the US. Consumers tend to avoid confronting the origins of their animal proteins to avoid cognitive dissonance related to animal suffering in large-scale factory farming entities from enterprises, preferring a "*romantic vision*" of the agricultural sector outlined as follows (Expert 7, Pos. 64):

> *„[Consumers] prefer [. . .]to construct this narrative in their head [. . .] of this lovely little farm where they're happy cows. And so, I think that that is used by the incumbent industry, too, as a form of protectionism to say: '[. . .]anybody who's criticiz-*

> *ing [. . .] dairy is criticizing your neighbor. You're [. . .] good small scale local farmer."'*, and points out, *"When really the biggest enemy to the small scale local daily dairy farmer for the last 30, 50 years has been large scale animal food production. [. . .]"*

As briefly mentioned in the preceding subsection, despite the EFSA's approval, the nations of the EU retain the power to vote on final market approval (Expert 5, Pos. 34). Concluding, the experts indicate that the ultimate market entry of novel foods derived from PF may still face socio-political resistance, regardless of verified safety and EE increases. Consequently, the decision to deny market entry to PF-derived products, influenced by misleading narratives about the agricultural sector as suggested by Experts 5 (Pos. 34; 38) and 7 (Pos. 50), represents a potential barrier.

Lack of Awareness

However, even when the products do reach the market, it is not clear how consumers will react. As described by Expert 7, who conducted expert studies on the question of consumer acceptance of PF-derived dairy products, products are still in a "pre-pre-consumer acceptance", even "pre-consumer understanding" phase (Pos. 48). A clear lack of awareness around the technology, its benefits, but also the presence of the problems it solves (e.g., lack of media coverage around agriculture's contribution to climate change (Expert 5, Pos. 40)) could lead to a lack of demand when entering the market, which would be an example of how the niche fails due to the market and user preferences of the established sociologist-technical regime.

This challenge extends beyond the food sector, touching other industries that interact with consumers. According to Expert 8 (Pos. 19), a large proportion of consumers lack the educational background required to comprehend complex issues related to chemistry, sustainability, and material performance. In combination with a lack of awareness around PF as a technology, this knowledge deficit leads to limited demand for PF-derived products.

The experts primarily criticize that despite the ambitions of establishing a bioeconomy within the EU, communication from politicians regarding measures to achieve this goal remains restrained (Expert 1, Pos. 17; Expert 5, Pos. 56). The use of industrial biotechnology as a potential climate technology receives disproportionately little attention compared to the contribution it can make to climate protection, especially when comparing it to political narratives surrounding other climate technologies, such as electric vehicles and alternative heating systems (Expert 1, Pos. 17).

As revealed from the interviews, one of the most significant barriers to the adoption of PF within the EU is the acceptance of products derived from this technology. Primarily, there's a lack of awareness about the technology's existence and potential, as well as an underestimation of the magnitude of the problems it aims to solve. There is currently no prevailing narrative highlighting how PF could contribute to solving environmental challenges and opening economic opportunities. Moreover, misunderstandings and uncertainties regarding the use of GMOs could lead to failures at critical points, such as obtaining final approval for novel foods from the European National Council, and more broadly, gaining consumer acceptance. If consumers fail to understand the benefits of PF products, they are unlikely to prefer and pay for them, a topic that is further explored in the following chapter.

4.2.3. Barrier VII: Price Lock-In

A *price lock-in* refers to a scenario where incumbent technologies persist due to their infrastructural, institutional, and economic advantages. Conversely, new, potentially more efficient, or sustainable technologies may face hurdles to gain market acceptance due to the price benefits of these established technologies (Geels, 2005; Unruh, 2000).

This scenario is particularly applicable to PF products in the commodity sector where they compete from a price-performance perspective with their traditional counterparts. While high-priced specialty molecules, like insulin, are almost entirely derived from PF, commodity molecules from PF often fail as they are too expensive to compete effectively (Expert 8, Pos. 25; Expert 4, Pos. 5). An additional cost for environmental benefits in the form of a green premium lacks willingness-to-pay on the market side as Expert 1 (Pos. 7; also, Expert 4, Pos 9) explains:

> *„[Molecules from PF] compete against chemistry [. . .] that has been optimized for scale and speed for decades or nearly a century. So, it's very tough to get to cost-parity. And [you can] rely on the green premium. So, you charge, let's say, 10%, 20 % or 100% more in terms of price to make up for the higher production costs. However, obviously, who's paying that as a downstream customer, if you still have the other option available, even if it is petrol chemistry based?"*

The experts note that these prices are significantly distorted. A contributing factor to the price lock-in is the skewed markets, especially in the agriculture sector and in the production of materials and fuels based on fossil fuels. Expert 5 (Pos. 52) criticizes the high level of subsidies in the agriculture sector, which ultimately benefits the selling prices of animal products. Expert 8 points out that the negative externalities of fossil fuel consumption are not adequately priced in, which further restricts the convergence of prices of material and fuel commodities from PF with their fossil-based counterparts Expert 8 (Pos. 39).

Hence, the phenomenon of price lock-in currently presents a barrier to the adoption of PF in commodity value chains of the EU economy, specifically in the sectors that are most significant for the transition to a bioeconomy.

4.3. Landscape Changes Open Up 'Windows of Opportunity'

For a careful analysis, it is important to separate changes on the landscape from the pressure they trigger and how this translates into changes in the socio-technical regime. Consequently, the structure of this work will present fundamental pressure points as 'Regime Destabilizations' in distinct subchapters, followed by the identification of clear 'Windows of Opportunity' that manifest for the niche, following the conceptual framework proposed by Geels (2002).

4.3.1. Driver IV: The Triple Planetary Crisis

The confluence of climate change, biodiversity loss, and pollution is driving a transformation in the socio-technical system. This shift exposes a series of potential windows of opportunity that innovative niches could tap into.

As the ecological and ethical consequences of contemporary production modalities become increasingly measurable and visible, a surge in scrutiny of these looming threats to planetary life in forthcoming decades is witnessed in both media and scholarly circles. This process is visible in media coverage and academic discourse, significantly advancing conversations about sustainability within societies of the European Union (Expert 1, Pos. 15; Expert 7; Pos. 60).

This movement, as per Expert 7, results in a "cultural discursive change" (Pos. 60), which subsequently shapes the objectives of influential organizations and stakeholders. In response, decision-makers and corporations within the EU recognize the need to recalibrate their operations towards sustainability (Expert 7, Pos. 60; Expert 1, Pos. 3).

This change also precipitates a shift in the environmental landscape, altering user and market preferences. The demand for products is increasingly tied to their perceived ecological sustainability (Expert 1, Pos. 15; Expert 7, Pos. 44; Expert 6, Pos. 19). This puts further pressure on manufacturing companies to adapt their value chain towards sustainability - and at the same time opens up opportunities for those who pay attention to it (Expert 1; Pos. 7).

Window of Opportunity I: Sustainability as a Performance Criterion

In light of landscape changes, incumbent businesses in the EU are now pressured to incorporate sustainability measures into their corporate strategies (Expert 6, Pos. 23; Expert 1, Pos. 3). Expert 1, as a strategy consultant, observes this particularly with companies whose business models are based on petrochemicals (fossil-based). He notices a strong demand for strategies on "how to get away from that" (Pos. 3). Expert 8 (Pos. 27) also emphasizes that a defossilization of the EU manufacturing sector is necessary to meet committed GHG reductions.

Consequently, companies based in the EU are pushing a range of sustainability initiatives (Expert 1, Pos. 3; Expert 6; Pos. 19). This shift opens up a window of opportunity for niche actors, especially for companies seeking to reduce negative environmental impact within their suuply chains (Expert 1; Pos. 23). The challenge for many of these companies is balancing the economic imperatives of growth and profitability with implementing ecological sustainability, a windows of opportunity niche innovations could tap into and trigger a paradigm shift, as Expert 1 (Pos. 3) describes from his experience consulting these companies on future strategies:

> *„Precision fermentation is obviously one [. . .] of the key workhorses that allow [. . .] clients to switch to synthesize their products more sustainably" (Expert 1, Pos. 3) as it would deliver the "[. . .]promise to break the trade-off between sustainability and profitability" (Expert 1, Pos. 15).*

As detailed in 4.1.1, it has become evident to a number of niche actors over recent years that their market entry strategies should be centered around consumer-driven, premium markets to leverage sustainability benefits despite a price premium (Expert 8; Pos. 25). Insights gathered from the diverse array of experts, including those from niche actors and incumbents, illustrate that the introduction of niche technologies, such as human-skin identical collagen in the cosmetics segment (see Expert 4), hinges on two intersecting dynamics. The first is the emergence of 'windows of opportunity' propelled by evolving user preferences and corporate aims in line with the shift towards sustainability (Expert 6, Pos. 19). The second element is the entrepreneurial acumen of PF niche actors, who, spurred by the developing dynamics, are proficient in capitalizing on these opportunities (see 4.1.1).

The potential for EE increases through the use of PF as a substitute for current production processes and ingredients paves the way for niche innovations to make successful market entries. This has been particularly effective in high-priced, consumer-centric markets where the advantage of EE and performance increase is evident, particularly when animal products are replaced with superior PF products (Expert 4, Pos. 7).

However, for commodities, it's challenging to justify the price premium needed in relation to the EE benefits. Here, experts see the need for regulators to provide additional support to these niches, a strategy which has proven effective, as detailed in the next chapter.

Window of Opportunity II: Regulators Push

The shift towards a stronger focus on sustainability at the landscape level is creating a multitude of windows of opportunity within the regulatory context. Policies have already been enacted to ban certain chemicals due to their toxicity, and the introduction of quotas is promoting demand of products from PF despite a price premium, as the example of biofuels shows. Legislators, as constituents of the current regulatory regime, are urged to craft policies within the manufacturing sector geared towards sustainability and environmental friendliness, and to tighten existing regulations. In response to these changes and in anticipation of further regulation, manufacturing companies are demonstrating an increased demand for products derived from PF.

Expert 8 (Pos. 25) describes how the introduction of regulations that impose sustainability criteria on products and industries, with a focus on CO_2 emissions, toxicity, and environmental impact, has opened positive windows of opportunity for niche players. This expert predicts that this will continue as these regulations are planned to be tightened. The company *LanzaTech*, for example, has found significantly better buyers for its fuels from PF since the introduction of biofuel quotas (Pos. 25). This could result in the transition from research to commercialization appearing more approachable for niches, despite the regime's price lock-in, and could prompt these niches to invest more pointedly and securely in strain optimization R&D and production, thereby strongly boosting niche accumulation.

Expert 1 underlines this, describing further regulations in the form of increased taxes on environmentally unfriendly production processes or products, as well as the introduction of quotas and subsidies for their bio-based counterparts, as necessary measures to *"level the playing field from a price point of view"*(Pos. 9).

Expert 8 (Pos. 15; 17) anticipates that current legislation, which already offers windows of opportunity for PF products, will be supplemented, and further enhanced by additional beneficial laws. Expert 3 (Pos. 57; 67) confirms this, stating that the decision-makers in EFSA are slowly yielding to the pressure on the landscape, described as an increasing "noise" in the regulatory environment, noticeable through public discourse, including internet forums. This is amplified as the legislative bodies of other governments, such as Singapore, Israel, and the USA, are advancing much more rapidly (Expert 3, Pos. 27). Also, niche entrepreneurs are trying to exert pressure on regulators, attempting to influence at the political level (Expert 8, Pos. 25).

In addition to the described change in consumer preferences and already occurring regulations, Expert 4 (Pos. 11) describes that companies are already looking for products with sustainability-optimized life-cycle-assessments in anticipation of further regulations:

> *"... [many large companies] now have their own teams focusing on GHG and with European regulation, they will be responsible for all those things. And that is changing now and wasn't relevant when we started but may be relevant in five years. [...] and I think regulation will push the other players in the same direction."*

In conclusion, the changes on the landscape triggered by ecological crises associated with human production and consumption are a significant driving force of niche accumulation. They fracture existing structures in the socio-technical regime at multiple points, creating an intertwined dynamic that opens spaces for niches. Based on expert interviews, it is anticipated that these spaces will only continue to widen as the situation intensifies.

4.3.2. Driver V: Need for Supply Chain Security & Diversification

The experts further describe that questions regarding food security for markets and populations are increasingly gaining relevance, provoking a scrutiny of the current socio-technical regime, and thereby fostering the exploration of potential alternatives (Expert 1, Pos. 15; Expert 2, Pos. 3; Expert 6, Pos. 23).

This pressure is expressed through both non-governmental global organizations like the United Nations (UN) with its World Food Programme, and governmental institutions including the EU, who seek to establish a food system that can sustainably provide adequate nourishment for all the earth's inhabitants, considering the challenges of hunger crises and a growing global population. This objective is embodied in the second Sustainable Development Goal of the UN, which aims to boost the productivity of global food supply and secure its long-term basis (Expert 1, Pos. 15; Expert 2, Pos. 3).

In addition, the EU has experienced multiple disruptions to supply chains in recent years, notably due to the COVID-19 pandemic and the war in Ukraine, highlighting the fragility and dependency of businesses that source products from abroad. Expert 6 (Pos. 23) describes the response of the affected incumbents as follows:

> *"Some of [EU manufacturing corporations] are in fact already looking to address it within their own supply chains. So, they are the ones asking for change because they are the ones realizing that, well, if all of my products contain sunflower oil and then there's a war in Ukraine, suddenly I have a big issue. So, I want to diversify where I'm getting my inputs from, and I want to make sure that that's a more resilient source."*

This observation provides a clear indication of geopolitical developments now leading to destabilizations in the regime, resulting in a quest for reducing supply chain dependencies and striving for more resilient value chains (Expert 2, Pos. 3).

Window of Opportunity III: Resilient Supply Chains & Independence

Expert 6 uses the example of the war in Ukraine to describe the disruption of food manufacturers' supply chains in the EU, illustrating how this opened up new opportunities for his portfolio companies using PF for food production (Pos. 25):

> *"So, some of the portfolio companies that we work with have had a good time during the Ukraine crisis, mostly because this was the first time that big food corporates actually opened up the ingredient list and actually started thinking about changing their recipe. Usually, they have a quite high bar for this. If all of a sudden price of sunflower and coconut oil goes up two or three times, then yes, now we can talk about, you know, a solution that might be able to replace these ingredients. So, for some of them, it creates opportunities [...]"*

This statement clearly suggests that established trade and thought patterns of the established industry regime are breaking up, and opportunities are arising that the niche, given sufficient momentum, can tap into. Particularly, the situation now opens up the possibility for start-ups to gain access to the pain points of incumbents, something that was previously denied to many due to ignorance of problems in processes and ingredients lists (Expert 4, Pos.29; c.f. 4.1.2).

Thus, exogenous factors such as geopolitical conflicts and other unforeseeable disruptions are clear drivers of the adoption of precision fermentation, as they break established sourcing practices of EU companies. Especially in times of uncertainty and price volatility, they highlight the benefits that precision fermentation can bring for the independence, resilience, and stability of manufacturing value chains.

Window of Opportunity IV: Competitive Moves Among Firms

As previously discussed, PF can serve as a competitive advantage for entrepreneurs, thanks to the shifting perception of sustainability as a performance criterion for consumers, enduring availability through resilient supply chains, and its status as non-subject to taxes and prohibitions or as the subject of subsidies. However, the potential performance benefits of products derived from PF extend beyond this. The capabilities of synthetic biology now allow us to engineer microbes that can produce familiar products of all kinds based on inexpensive substrates, possibly even waste or emissions. (Expert 8, Pos. 31).

Moreover, it is now possible to create previously unknown, novel molecules with unprecedented properties that outperform existing products. Expert 1 highlights the significant strides made in the field due to contributions from *DeepMind* and *Meta* and their *Generative AI*[10] algorithms such as *AlphaFold 2*[11]. These entities have provided a vast number of predicted protein structures that, despite not being proven, are expected to be highly accurate. This development has facilitated a stronger connection between sequence information and function, accelerating the discovery of molecules with novel functions and the genetic sequence necessary to synthetize them (Expert 1, Pos. 13).

Even companies not primarily concerned with sustainability aspects associated with the transition to PF can leverage this technology to their advantage. This becomes particularly relevant when industry external players use the technological means to conduct PF, opening a new market and challenging incumbents with superior versions of the product. Expert 4 (Pos. 29) describes their business development learnings:

> *"So, if I work with a traditional [target molecule] employer, I probably won't open a new market for them. They have all the distribution networks; they have all the partners and so on. But in a sense I'm competing internally, whereas if I go to another company who's running familiar with my kind of technology, but they don't have any current market access right now and they're kind of a prime partner, [. . .]. And also, you know, I'm helping them enter a new market in that way."*

Hence, the introduction of PF technology has the potential to not only counter the effects of unsustainable practices but also to provide competitive advantages for both established players and newcomers. This creates a multitude of windows of opportunity across various segments for niche actors, either through collaboration with existing incumbents or by establishing markets for new entrants.

5. Discussion

Building upon Frank Geels' (2002) theoretical framework, which contextualizes system innovation adoption, it is apparent that TTs are not isolated events in a technological vacuum. They are deeply embedded within societal fabric, reflecting the values, interests, and power dynamics of the society in which they develop (Geels, 2002). This necessitates a comprehensive understanding among all actors within the established socio-technical system—including policymakers, established industry, users, and markets within the EU—of the potential role of PF in realizing the economic and ecological targets stipulated in The European Green New Deal (2019) and EU's Bioeconomy Strategy (2018).

However, the interview findings suggest that despite PF's potential, a robust awareness and understanding of it have yet to penetrate the socio-technical establishment (Chapter 4.2.2). Concurrently, other global economies are advancing their biomanufacturing strategies and reaping their associated benefits.

For instance, the Biden-Harris administration in the United States (USA) introduced the "New Bold Goals and Priorities to Advance American Biotechnology and Biomanufacturing" on March 22, 2023. This initiative, following an Executive Order signed in September 2022, underscores the importance of biomanufacturing, including PF, in addressing significant societal objectives (The White House Office of Science and Technology Policy, 2023). These objectives comprise: *1) climate change solutions, 2) food and agricultural innovation, 3) supply chain resilience, 4) human health, and 5) cross-cutting advances*.

In response to this recognition, the USA has implemented, or plans to implement, a series of policy measures designed to elevate biomanufacturing as a key pillar of the US economy. Such measures include collaborations between the state and private enterprises, and the investment and promotion of biomanufacturing capabilities and innovation. A review of these goals suggests a striking resemblance to the objectives outlined by the EU in the aforementioned reports.

[10] Generative artificial intelligence refers to an algorithmic system that is capable of creating new content (Yang et al., 2017).

[11] AlphaFold 2 is an artificial intelligence network developed by DeepMind that uses deep learning algorithms to predict the 3D structure of proteins from their amino acid sequences (Jumper et al., 2021).

However, a key distinction arises in the approach. While the USA views biomanufacturing as a central driver in achieving these goals and is actively working to accelerate its uptake, the EU's approach appears to lack sufficient understanding of the potential, needs, drivers, and challenges of niche technologies, as indicated in the interviews. This gap in understanding suggests that recognizing the role of biomanufacturing in meeting a range of critical goals is a prerequisite for effective policy action. This understanding appears to be growing within the EU, especially as other economies make strategic advances, as indicated by Expert 3 (Pos. 27). However, this growing awareness is yet to translate into concrete policies.

In this context, the ensuing discussion will endeavor to highlight potential levers for the acceleration of a bioeconomy powered by biomanufacturing. Drawing from the drivers and barriers identified in Chapter 4, it will also offer actionable recommendations for the most influential stakeholders, primarily policymakers, but also industry incumbents and niche actors.

5.1. Deriving Policy Recommendations

Drawing on Geels' (2006), an effective transition policy strategy must exhibit two key attributes. First, it should apply increased pressure on the existing regime, potentially by employing financial tools and regulations. Second, it should foster the development of groundbreaking innovations within niches.

The implementation and effectiveness of measures depend fundamentally on the prevailing narrative that embeds the vision of a bioeconomy, its benefits, and the necessary steps for its realization into the minds of the regime's stakeholders. Only then will policy recommendations be discussed, implemented, and resonate with the actors within the regime. Thus, it is considered essential that any introduced policy recommendations, whether they aim to promote niches or regulate existing processes, are surrounded by a narrative that emphasizes their relevance and value.

On this basis, measures can be suggested and initiated, aligning socio-technical regime incumbents, users, markets, and niche actors towards the same vision of a bioeconomy in the EU. This alignment will ensure that ecological and economic objectives are jointly pursued and achieved. This unity in direction and purpose not only enhances the efficiency of initiatives but also increases the likelihood of their acceptance and success.

Technological Barriers

The interviews reveal that advancements in synthetic biology have substantially contributed to niche momentum, enabling some niches to even take over entire markets, while others have managed to at least gain market entry. To further cultivate a) an industry based on biomanufacturing for economic growth and improved performance of the deployed molecules, and b) a circular economy that achieves ecological goals through the use of cost-effective, renewable feedstocks, targeted R&D efforts should be initiated and funded. These R&D efforts should primarily conduct basic research to expand the capabilities of synthetic biology. This includes increasing the flexibility of inputs and outputs in fermentation processes, optimizing strains for market viability of drop-in molecules, exploring the feasibility of producing new molecules with better properties, and considering the use of next-generation feedstocks from industrial waste streams. The technology developed from this research should then be made broadly accessible to a range of stakeholders in both universities and industry to enhance niche market growth.

It's important to note that these R&D activities need not be limited to universities or research institutions. The European Institute of Innovation and Technology already puts out tenders that businesses, including technology-focused start-ups, can apply for. Besides traditional research grants, tenders in synthetic biology could initiate relevant R&D efforts in the EU and provide guidance to niche players on the most pressing issues for governments and corporations, a current major barrier as described in Chapter 4.1.3. As Expert 4 (Pos. 39) lines out, this could encourage companies to focus on solving real-world problems and generating revenue through their innovations.

The potential use of next-generation feedstocks, especially in line with advancements in substrate engineering, is closely tied to their availability and suitability. Therefore, policymakers should also focus on identifying future supply sources, establishing storage facilities, and developing treatment plants within the EU. If these infrastructures do not currently exist, it is up to policymakers to facilitate their creation.

Commercialization Barriers

Chapter 4.1.3 highlights the lack of transition from research activities to commercial practice. Fostering collaboration between universities and established industry players could help bridge this gap. Universities should be considered not only as centers of knowledge creation but also as engines for technological advancement and innovation, including the creation of spin-offs. This implies fostering an ecosystem that enables academics to engage in entrepreneurial ventures. Also, incentives for academics to collaborate with industry partners can be a promising approach, as well as equipping universities with resources to develop programs and support structures that nurture entrepreneurship.

Furthermore, while public funding programs often provide the financial means necessary for research and development, they frequently lack the guidance and mentorship that researchers need to convert their scientific ideas into viable businesses. Therefore, funding programs and tenders could contemplate incorporating components of mentorship and guidance alongside financial support. This holistic approach could enhance the effectiveness of the funding, accelerating the journey from laboratory discoveries to marketable solutions.

Infrastructure Barriers

As discussed in Chapter 4.1.3, start-ups, particularly niche actors, grapple with a lack of fermentation capacity in the EU. An essential research question arising from this concerns the development of solutions to bridge this gap. According to Experts 1 and 5, the role of EU nations or the EU itself is instrumental as a financier and creator of infrastructure to facilitate scale-up attempts within strain optimization loops and commercialization efforts, contingent on rental payments. It should be in the EU's interest to provide adequate infrastructure for both R&D and commercialization - either by direct intervention or through fostering innovations and private market partnerships that enable this. The construction of fermentation facilities by niche actors could also be further promoted with grants or favorable loans.

Regulatory Barriers

The hurdles described in 4.2.1, particularly for PF niche actors in the food sector regarding the approval process, pose a significant barrier to market entry for novel food niche technologies in the EU. To prevent a drain of Novel Food companies along with their talents, proprietary knowledge, and economic potential, the EFSA must fundamentally clarify the process of novel food approval. The first step involves drafting clear guidelines for various types of food innovations, indicating what is required for navigation through the process. There also needs to be clarity, especially in the context of GMOs on which process is most suitable for the respective product. Through clear milestones with predefined submissions and timelines, uncertainty should be reduced, time-to-market accelerated, and credibility boosted with potential investors and partners. As exemplified by Expert 5 (Pos. 34) in Singapore's approach, dedicated teams that actively guide niche technology actors through the approval process and promote R&D as well as infrastructure projects with grants, are needed to attract the best talents, companies, and products. While the EU should continue prioritizing the health of its citizens by only approving safe foods, GMO or non-GMO, faster, cooperative processes can still achieve this balance between safety and innovation.

Price Lock-in Barrier

The promotion of bioethanol uptake through quotas, as described by Expert 8 (Pos. 25), has been a significant measure to provide more certainty to producers of such products for the further development of their companies and platforms. To further encourage the adoption of PF products, such quotas should be expanded, giving the niche more assurance of product uptake, momentum, and credibility. At the same time, it would be necessary to properly price the actual externalities of fossil-based and animal-derived products, meaning the damages caused primarily by GHG emissions and environmental pollution. This would counteract the market distortions currently described. The same applies to the partially reduced taxation of milk and meat products, as well as substantial agricultural subsidies. While these are connected to considerations of promoting and maintaining the current societal and economic system, a gradual convergence of the prices of traditionally manufactured products with potentially subsidized PF ones is recommended until price parity is achieved without disrupting economic and societal systems.

Cultural and Psychological Factors

As discussed in Chapter 4.2.2, current cultural and psychological factors pose relevant barriers to the adoption of PF. Appropriate public education and awareness campaigns should be implemented to address these concerns.

The application of GMOs in food and feed is a complex and often misunderstood topic, capable of arousing apprehension among consumers, voters, and policymakers alike. Historical misuse of GMOs has led to undesirable outcomes, contributing to skepticism about this technology. However, like any powerful technology, it requires a secure framework for sensible application. Accordingly, the narrative around GMOs needs to be reframed to emphasize that, in the context of PF, they are subject to the same regulatory criteria as other food products. This would assure their safe use while harnessing the benefits of this production method.

The interviews with Experts 7 and 8 also highlighted a fundamental lack of understanding of the technology behind PF. As a result, novel products that are, for example, neither plant-based milk alternatives nor animal milk can cause confusion among consumers. Complex chemicals and materials, whose production processes and environmental implications are not easily understood, may deter consumers from recognizing the environmental benefits of PF alternatives. This lack of understanding could prevent demand, despite a potential willingness to pay a green price premium.

Legislation could support in this regard by promoting awareness and narratives around the bioeconomy, biomanufacturing, and PF. Furthermore, clear regulations regarding the labeling of products with respect to their environmental impact could be made mandatory, thereby making the processes behind the products more visible. Such initiatives could facilitate better consumer understanding, leading to more informed decision-making, and ultimately contributing to the wider acceptance and adoption of PF technologies.

In collaboration with citizens, communities, and businesses of all sizes, the European Union should explore the extent to which goods and food production in the bioeconomy should be centralized. Socio-political factors, such as concerns about the displacement of small businesses, can become an obstacle if products from PF are rejected by markets, consumers, and also within the European Council. These concerns should be taken seriously and should be accompanied by a positive narrative about creating a more ecologically, economically, and socially sustainable form of economy.

5.2. Considerations for Industry Incumbents

For incumbent companies within the regime, the technological and entrepreneurial momentum of the niche represents both an opportunity and a threat. Companies made aware of the fragility of their supply chains in the wake of the Covid pandemic and the Russian invasion of Ukraine have a chance to become more independent from global supply chains through metabolic engineering. At the same time, synthetic biology offers companies that seek to give their products new properties, the opportunity to develop a competitive edge by designing de novo molecules.

As Expert 6 (Pos. 7) puts it: *"[...] corporations obviously have a hand on the steering wheel. They can either in-source these technologies and centralize the way biomanufacturing happens, or they can choose to ignore it and be disrupted"* - not necessarily by start-ups, but by neighboring regime incumbents partnering with niche actors. The technology paves the way for the entry of new competitors, not only from the niche but also from neighboring regimes - companies that have the infrastructure and talent to carry out large-scale biomanufacturing processes could today produce their current core product, and tomorrow that of a foreign industry - possibly even harnessing potential advantages of synthetic biology along price-performance dimensions.

For incumbents, the consideration is therefore to interact more intensively with the niche in order to identify potentially threatening trends and harness possible opportunities. Key levers for this could be the following:

- Establishing confidential partnerships with niche actors, showcasing the current pain points are clearly and explicitly linked with possible improvement objectives. This gives niche actors guidance on how best to use their technology to solve internal problems of the regime and resolves communication mismatches. At the same time, it reduces market risk for them and makes them appear more credible to VC and focus only on technology challenges.
- Providing an interdisciplinary team that has the know-how, infrastructure, time, and resources to scale up laboratory innovations, but also to market them appropriately and actively work on collaboration projects in the niche and with other niche actors.
- Actively embracing the possibilities of biomanufacturing by anticipating further regulations and the EU bioeconomy strategy, and actively co-shaping policies and structures. Furthermore, observing international movements towards bioeconomy and biomanufacturing and thus utilizing windows to become a significant player as an exporter of intellectual property and infrastructure in the future.

5.3. Considerations for Entrepreneurial Niche Actors

Entrepreneurs in the niche face many challenges in navigating through the aforementioned barriers. Essential for navigating towards commercialization and overcoming the so-called 'Valley of Death' is building credibility with investors, corporate partners, and potential regulatory authorities that may promote selected companies within the context of possible policies. Establishing this credibility requires a delicate balancing act between aligning with the needs of the current regime while maintaining one's own vision. As some of the described entrepreneurs have learned, companies risk failure with their efforts if they push products into the market without corresponding demand. Alongside technical development, a commercial acumen is necessary, that guide business development towards customer segments that can be captured given current price-performance possibilities of the technology. Potential market entry opportunities to prove the potential of one's technology and build credibility are not necessarily in the initially targeted market – however they can be great showcases to build trusted partnerships upon, may it be to customers, corporate partners, or CMOs.

In the context of MLP, it is essential for niche actors to actively leverage the pressures of the landscape. While there are numerous opportunities for market entry among both consumers and corporate customers, it often appears that there is a lack of awareness of the benefits of synthetic biology across dimensions such as sustainability, ethical consumption, resilience, and performance improvements – leading to a lack of understanding and demand. Niche actors should strive to actively raise awareness for a narrative of their technology within the framework of an inclusive bioeconomy, in order to further open cracks in the regime into windows of opportunity.

5.4. Limitations and Suggestions for Further Research

This thesis focuses specifically on one major technology of biomanufacturing: PF. Its potential to transform value chains across sectors and contribute significantly to the transition to a bioeconomy warrants particular attention. However, the diverse sub-technologies of synthetic biomanufacturing differ substantially in their drivers and barriers, necessitating separate analyses despite their collective contribution to the bioeconomy transition. Consequently, a major limitation of this thesis is the exclusion of other technologies that could contribute to the transition within the EU. This extends beyond synthetic biology-based technologies to those rooted in thermochemical, chemical, and mechanical processes. It is crucial to recognize that PF is only one of several technological forces driving the creation of a bioeconomy, and therefore conducting research on the adoption of its peers is of high relevance.

The author has a limited understanding of the nuances and complexities involved in actual policy-making processes. Policymaking is a multifaceted field, influenced by intricate stakeholder relationships, power dynamics, historical contexts, and unique national or regional characteristics. The proposals put forward in this study largely center around the development and implementation of precision fermentation as a platform technology, thereby neglecting to address the broader spectrum of EU and global politics. These politics encompass aspects such as trade agreements, geopolitical relations, and multilateral regulations. This focus, while narrow, could potentially neglect certain factors that may emerge in real-world policy-making scenarios, such as possible trade-offs, wider systemic impacts, or socio-political consequences. To address these limitations, future research and policy measures should ideally involve collaboration with experts in policy-making and political science, to ensure a comprehensive understanding of the wider political context when discussing precision fermentation and similar platform technologies.

Additionally, the selection of interview partners is limited to eight individuals in interviews often lasting no more than an hour. While unique insights can be gained by comparing experts' answers, these interviews only provide a brief glimpse into the dynamics of the processes. A more holistic approach would require further in-depth conversations with various stakeholders within the regime and niche, including those from different sectors and regions. A key aspect of this was the intention to interview an expert who is a practicing engineer in the field. Regrettably, none of the potential interviewees identified for this purpose responded to the outreach emails.

Moreover, the MLP framework may place excessive emphasis on technological aspects of transitions, downplaying the role of social, cultural, and political dimensions in shaping PF adoption. This is especially relevant considering the considerable differences among EU member states in these dimensions. By focusing on the EU with the EC, national-level differences within the EU may be neglected. It is important to examine how these differences might impact the adoption of PF technologies across Europe and therefore raises relevant windows for future research. Further research could aim to explore the perspectives and experiences of a broader array of stakeholders within both the regime and niche sectors.

The MLP framework does not explicitly address the role of power dynamics in shaping socio-technical transitions. In the context of this thesis, the varying degrees of influence stakeholders have over the adoption of PF technologies is particularly significant. On the one hand, the framework inadequately considers power dynamics; on the other, reliable information and expert knowledge are lacking regarding which drivers and challenges ultimately shape the transition and to what extent. Some aspects and unanswered questions remain among the experts. Furthermore, conceptualizing the MLP can be challenging, particularly when measuring and quantifying interactions across levels, which may limit the comparability and applicability of the findings. A deeper exploration of power dynamics and their influence on the transition process could strengthen the analysis.

Conceptualizing the MLP can be challenging, particularly in terms of measuring and quantifying interactions across levels. This complexity may hinder the comparability and applicability of the findings, as it requires a nuanced understanding of the interplay between various system components. Consequently, future research may benefit from developing more refined methodologies to capture these interactions, ensuring a more robust analysis and facilitating comparisons across different studies. Also, to derive concrete policy recommendations, actions, and their concrete effects should be quantified.

The subject matter of this thesis is inherently complex, multi-layered, and detailed, spanning several industry sectors influenced by the same technology. Attempting to develop a comprehensive perspective within this context is a demanding task, and each issue examined raises additional questions. While these questions are highly relevant to the acceleration of the transition, addressing them is beyond the scope of this thesis. Further research is essential to explore these intricacies and contribute to a deeper understanding of the factors driving the transition to a bioeconomy powered by PF.

6. Conclusion

The EU finds itself at a critical crossroads in shaping the trajectory of its economy in the face of the triple planetary crisis. Driven by the technological trajectory of synthetic biology, a vibrant ecosystem has developed within the biomanufacturing niche, working assiduously to influence EU markets with noteworthy momentum. Sustainability pressures and unexpected global supply chain disruptions are fracturing entrenched structures, thereby creating opportunities to stimulate niche momentum. However, a multitude of internal barriers at the niche and socio-technical regime levels obstruct the initiation of a comprehensive transformation process. Given the identified barriers concerning infrastructure, regulation, market interventions, and lack of awareness, it appears imperative for policymakers to facilitate a transformative process. It is now up to EU decision-makers to consider the extent to which biomanufacturing can be part of a vision for a European bioeconomy and to deliberate, in consultation with communities and incumbents, how this can be structured. Utilizing the MLP, this study has been able to highlight the most influential interdisciplinary drivers and barriers. While the proposed policy recommendations provide broad directions for potential actions, they are subject to limitations. Future research should delve into these barriers and drivers in detail, examining how they must be addressed to accelerate the transition to a bioeconomy.

References

Auerswald, P. E., & Branscomb, L. M. (2003). Valleys of Death and Darwinian Seas: Financing the Invention to Innovation Transition in the United States. *The Journal of Technology Transfer*, *28*(3–4), 227–239. https://ideas.repec.org/a/kap/jtecht/v28y2003i3-4p227-39.html

Barnett, J. A. (2003). Beginnings of Microbiology and Biochemistry: The Contribution of Yeast Research. *Microbiology*, *149*(3), 557–567. https://doi.org/10.1099/MIC.0.26089-0/CITE/REFWORKS

Blank, S. (2022). Entrepreneurs, Is a Venture Studio Right for You? *Harvard Business Review*. https://hbr.org/2022/12/entrepreneurs-is-a-venture-studio-right-for-you

Braun, V., & Clarke, V. (2012). Thematic Analysis. In *APA Handbook of Research Methods in Psychology: Vol. Volume 2* (pp. 57–71). American Psychological Association. https://doi.org/10.1037/13620-004

Bugge, M., Hansen, T., & Klitkou, A. (2016). What Is the Bioeconomy? A Review of the Literature. *Sustainability*, *8*(7), 691. https://doi.org/10.3390/su8070691

Cameron, D. E., Bashor, C. J., & Collins, J. J. (2014). A Brief History of Synthetic Biology. *Nature Reviews Microbiology*, *12*(5), 381–390. https://doi.org/10.1038/nrmicro3239

Carbonell, P., Jervis, A. J., Robinson, C. J., Yan, C., Dunstan, M., Swainston, N., Vinaixa, M., Hollywood, K. A., Currin, A., Rattray, N. J. W., Taylor, S., Spiess, R., Sung, R., Williams, A. R., Fellows, D., Stanford, N. J., Mulherin, P., Le Feuvre, R., Barran, P., & Scrutton, N. S. (2018). An Automated Design-Build-Test-Learn Pipeline for Enhanced Microbial Production of Fine Chemicals. *Communications Biology*, *1*(1), 1–10. https://doi.org/10.1038/s42003-018-0076-9

Chai, K. F., Ng, K. R., Samarasiri, M., & Chen, W. N. (2022). Precision Fermentation to Advance Fungal Food Fermentations. *Current Opinion in Food Science*, *47*, 100881. https://doi.org/10.1016/J.COFS.2022.100881

Cheng, A. A., & Lu, T. K. (2012). Synthetic Biology: An Emerging Engineering Discipline. *Annual Review of Biomedical Engineering*, *14*, 155–178. https://doi.org/10.1146/annurev-bioeng-071811-150118

Clarysse, B., Wright, M., & Van de Velde, E. (2011). Entrepreneurial Origin, Technological Knowledge, and the Growth of Spin-Off Companies. *Journal of Management Studies*, *48*(6), 1420–1442. https://doi.org/10.1111/j.1467-6486.2010.00991.x

Cohen, S. N., Chang, A. C. Y., Boyer, H. W., & Helling, R. B. (1973). Construction of Biologically Functional Bacterial Plasmids In Vitro. *Proceedings of the National Academy of Sciences of the United States of America*, *70*(11), 3240–3244. https://doi.org/10.1073/PNAS.70.11.3240

Demain, A. L., & Adrio, J. L. (2008). Contributions of Microorganisms to Industrial Biology. *Molecular Biotechnology*, *38*(1), 41–55. https://doi.org/10.1007/s12033-007-0035-z

Dobell, C. (1932). Antony van Leeuwenhoek and His "Little Animals": Being Some Account of the Father of Protozoology and Bacteriology and His Multifarious Discoveries in These Disciplines. *Nature*, *130*(3288), 679–680. https://doi.org/10.1038/130679a0

Elzen, B., Geels, F. W., & Green, K. (2004). System Innovation and the Transition to Sustainability. In B. Elzen, F. W. Geels, & K. Green (Eds.), *System Innovation and the Transition to Sustainability*. Edward Elgar Publishing. https://doi.org/10.4337/9781845423421

European Commission. (n.d.-a). Genetically Modified Organisms. Retrieved May 21, 2023, from https://food.ec.europa.eu/plants/genetically-modified-organisms_en

European Commission. (n.d.-b). Novel Food. Retrieved May 21, 2023, from https://food.ec.europa.eu/safety/novel-food_en

European Commission. (2018). *EU Bioeconomy Strategy Progress Report* (tech. rep.). https://doi.org/10.2777/997651

European Commission. (2019). The European Green Deal. https://eur-lex.europa.eu/resource.html?uri=cellar:b828d165-1c22-11ea-8c1f-01aa75ed71a1.0002.02/DOC_1&format=PDF

Fleming, A. (1929). On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to their Use in the Isolation of B. influenzæ. *British Journal of Experimental Pathology*, *10*(3), 226. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2048009/

Flores Bueso, Y., & Tangney, M. (2017). Synthetic Biology in the Driving Seat of the Bioeconomy. *Trends in Biotechnology*, *35*(5), 373–378. https://doi.org/10.1016/j.tibtech.2017.02.002

Geels, F. W. (2002). Technological Transitions as Evolutionary Reconfiguration Processes: A Multi-Level Perspective and a Case-Study. *Research Policy*, *31*(8–9), 1257–1274. https://doi.org/10.1016/S0048-7333(02)00062-8

Geels, F. W. (2005). Processes and patterns in transitions and system innovations: Refining the co-evolutionary multi-level perspective. *Technological Forecasting and Social Change*, *72*(6 SPEC. ISS.), 681–696. https://doi.org/10.1016/J.TECHFORE.2004.08.014

Geels, F. W. (2006). Multi-Level Perspective on System Innovation: Relevance for Industrial Transformation. In *Understanding Industrial Transformation* (pp. 163–186). Kluwer Academic Publishers. https://doi.org/10.1007/1-4020-4418-6_9

Geels, F. W., & Schot, J. (2007). Typology of sociotechnical transition pathways. *Research Policy*, *36*(3), 399–417. https://doi.org/10.1016/J.RESPOL.2007.01.003

Goeddel, D. V., Kleid, D. G., Bolivar, F., Heyneker, H. L., Yansura, D. G., Crea, R., Hirose, T., Kraszewski, A., Itakura, K., & Riggs, A. D. (1979). Expression in Escherichia coli of chemically synthesized genes for human insulin. *Proceedings of the National Academy of Sciences*, *76*(1), 106–110. https://doi.org/10.1073/pnas.76.1.106

InFamily Foods. (n.d.). InFamily Foods. Retrieved May 19, 2023, from https://infamily-foods.com/de/

IPCC. (2023). Synthesis Report of the IPCC Sixth Assessment Report (AR6 SYR) - Summary for Policymakers. *In Diriba Korecha Dadi. Panmao Zhai*.

Jumper, J., Evans, R., Pritzel, A., Green, T., Figurnov, M., Ronneberger, O., Tunyasuvunakool, K., Bates, R., Žídek, A., Potapenko, A., Bridgland, A., Meyer, C., Kohl, S. A. A., Ballard, A. J., Cowie, A., Romera-Paredes, B., Nikolov, S., Jain, R., Adler, J., et al. (2021). Highly accurate protein structure prediction with AlphaFold. *Nature*, *596*(7873), 583–589. https://doi.org/10.1038/s41586-021-03819-2

Keasling, J. D. (2010). Manufacturing Molecules Through Metabolic Engineering. *Science*, *330*(6009), 1355–1358. https://doi.org/10.1126/SCIENCE.1193990

Kemp, R., Schot, J., & Hoogma, R. (1998). Regime shifts to sustainability through processes of niche formation: The approach of strategic niche management. *Technology Analysis and Strategic Management*, *10*(2), 175–198. https://doi.org/10.1080/09537329808524310

Ko, Y.-S., Kim, J. W., Lee, J. A., Han, T., Kim, G. B., Park, J. E., & Lee, S. Y. (2020). Tools and strategies of systems metabolic engineering for the development of microbial cell factories for chemical production. *Chemical Society Reviews*, *49*(14), 4615–4636. https://doi.org/10.1039/D0CS00155D

Korhonen, J., Honkasalo, A., & Seppälä, J. (2018). Circular economy: The concept and its limitations. *Ecological economics*, *143*, 37–46.

Lane, N. (2015). The unseen World: Reflections on Leeuwenhoek (1677) 'Concerning little animals.' *Philosophical Transactions of the Royal Society B: Biological Sciences*, *370*(1666), 20140344. https://doi.org/10.1098/RSTB.2014.0344

Lips, D. (2022). Fuelling the future of sustainable sugar fermentation across generations. *Engineering Biology*, *6*(1), 3–16. https://doi.org/10.1049/ENB2.12017

Liu, Z., Wang, K., Chen, Y., Tan, T., & Nielsen, J. (2020). Third-generation biorefineries as the means to produce fuels and chemicals from CO2. *Nature Catalysis*, *3*(3), 274–288. https://doi.org/10.1038/s41929-019-0421-5

Luscombe, N. M., Greenbaum, D., & Gerstein, M. (2001). What is bioinformatics? A proposed definition and overview of the field. *Methods of Information in Medicine*, *40*(4), 346–358. https://doi.org/10.1055/s-0038-1634431

McGovern, P. E., Zhang, J., Tang, J., Zhang, Z., Hall, G. R., Moreau, R. A., Nuñez, A., Butrym, E. D., Richards, M. P., Wang, C., Cheng, G., Zhao, Z., & Wang, C. (2004). Fermented beverages of pre- and proto-historic China. *Proceedings of the National Academy of Sciences*, *101*(51), 17593–17598. https://doi.org/10.1073/pnas.0407921102

Meuser, M., & Nagel, U. (1991). ExpertInneninterviews — vielfach erprobt, wenig bedacht. *Qualitativ-Empirische Sozialforschung*, 441–471. https://doi.org/10.1007/978-3-322-97024-4_14

Monbiot, G. (2022). Embrace what may be the most important green technology ever. It could save us all. *The Guardian*. https://www.theguardian.com/commentisfree/2022/nov/24/green-technology-precision-fermentation-farming

Morales, M., Quintero, J., Conejeros, R., & Aroca, G. (2015). Life cycle assessment of lignocellulosic bioethanol: Environmental impacts and energy balance. *Renewable and Sustainable Energy Reviews*, *42*, 1349–1361. https://doi.org/10.1016/J.RSER.2014.10.097

Mutalik, V. K., Guimaraes, J. C., Cambray, G., Lam, C., Christoffersen, M. J., Mai, Q.-A., Tran, A. B., Paull, M., Keasling, J. D., Arkin, A. P., & Endy, D. (2013). Precise and reliable gene expression via standard transcription and translation initiation elements. *Nature Methods*, *10*(4), 354–360. https://doi.org/10.1038/nmeth.2404

Nielsen, J., & Keasling, J. D. (2016). Engineering Cellular Metabolism. *Cell*, *164*(6), 1185–1197. https://doi.org/10.1016/J.CELL.2016.02.004

Osawa, Y., & Miyazaki, K. (2006). An empirical analysis of the valley of death: Large-scale R&D project performance in a Japanese diversified company. *Asian Journal of Technology Innovation*, *14*(2), 93–116. https://doi.org/10.1080/19761597.2006.9668620

Pandey, A., Tyagi, R. D., & Varjani, S. (2021). *Biomass, Biofuels, Biochemicals* (1st). Elsevier. https://doi.org/10.1016/C2019-0-04356-7

Papagianni, M. (2007). Advances in citric acid fermentation by Aspergillus niger: Biochemical aspects, membrane transport and modeling. *Biotechnology Advances*, *25*(3), 244–263. https://doi.org/10.1016/J.BIOTECHADV.2007.01.002

Perfect Day & WSP USA. (2021). ISO-Conformant Report: Comparative Life Cycle Assessment of Perfect DayWhey Protein Production to Dairy Protein. https://www.perfectdayfoods.com/resources/perfect-day-life-cycle-assessment/

Poore, J., & Nemecek, T. (2018). Reducing food's environmental impacts through producers and consumers. *Science*, *360*(6392), 987–992. https://doi.org/10.1126/SCIENCE.AAQ0216

Raven, R. P. J. M. (2004). Implementation of manure digestion and co-combustion in the Dutch electricity regime: A multi-level analysis of market implementation in the Netherlands. *Energy Policy*, *32*(1), 29–39. https://doi.org/10.1016/S0301-4215(02)00248-3

Ross, P. R., Morgan, S., & Hill, C. (2002). Preservation and fermentation: past, present and future. *International Journal of Food Microbiology*, *79*(1–2), 3–16. https://doi.org/10.1016/S0168-1605(02)00174-5

Ruiz, P., Skoczinski, P., Raschka, A., Hark, N., & Carus, M. (2023). *Carbon Dioxide (CO2) as Feedstock for Chemicals, Advanced Fuels, Polymers, Proteins and Minerals – Technologies and Market, Status and Outlook, Company Profiles*. https://doi.org/10.52548/HKBS8158

Soleymani Angili, T., Grzesik, K., Rödl, A., & Kaltschmitt, M. (2021). Life Cycle Assessment of Bioethanol Production: A Review of Feedstock, Technology and Methodology. *Energies*, *14*(10), 2939. https://doi.org/10.3390/EN14102939

The Good Food Institute. (2023). 2022 Fermentation State of the Industry Report. https://www.gfi.org

The White House Office of Science and Technology Policy. (2023). Bold Goals for U.S. Biotechnology and Biomanufacturing. https://www.whitehouse.gov/ostp

UNCCD. (2022). Global Land Outlook, Second Edition – Summary for Decision Makers.

UNEP. (2022). Annual Report 2022. https://www.unep.org

Unruh, G. C. (2000). Understanding carbon lock-in. *Energy Policy*, *28*(12), 817–830. https://doi.org/10.1016/S0301-4215(00)00070-7

Venkata Mohan, S., Modestra, J. A., Amulya, K., Butti, S. K., & Velvizhi, G. (2016). A Circular Bioeconomy with Biobased Products from CO2 Sequestration. *Trends in Biotechnology*, *34*(6), 506–519. https://doi.org/10.1016/J.TIBTECH.2016.02.012

Verbong, G., & Geels, F. (2007). The ongoing energy transition: lessons from a socio-technical, multi-level analysis of the Dutch electricity system (1960-2004). *Energy Policy*, *35*(2), 1025–1037. https://doi.org/10.1016/J.ENPOL.2006.02.010

Vivien, F.-D., Nieddu, M., Befort, N., Debref, R., & Giampietro, M. (2019). The Hijacking of the Bioeconomy. *Ecological Economics*, *159*, 189–197. https://doi.org/10.1016/J.ECOLECON.2019.01.027

Walsh, G. (2005). Therapeutic insulins and their large-scale manufacture. *Applied Microbiology and Biotechnology*, *67*(2), 151–159. https://doi.org/10.1007/s00253-004-1809-x

Weterings, R., Kuijper, J., Smeets, E., Annokkée, G. J., & Minne, B. (1997). *81 mogelijkheden voor duurzame ontwikkeling*. The Hague: Ministry of VROM.

World Bank. (2023). GDP growth (annual %). https://data.worldbank.org/indicator/NY.GDP.MKTP.KD.ZG

Yang, Y. J., Holmberg, A. L., & Olsen, B. D. (2017). Artificially Engineered Protein Polymers. *Annual Review of Chemical and Biomolecular Engineering*, *8*, 549–575. https://doi.org/10.1146/annurev-chembioeng-060816-101620

Zhang, C., Ottenheim, C., Weingarten, M., & Ji, L. (2022). Microbial Utilization of Next-Generation Feedstocks for the Biomanufacturing of Value-Added Chemicals and Food Ingredients. *Frontiers in Bioengineering and Biotechnology*, *10*, 486. https://doi.org/10.3389/fbioe.2022.874612